EPA Jacket 2517-85

Vol.2

Caring for pets since 1868
Sergeant's®
Sergeant's Pet Care Products, Inc.
2625 South 158th Plaza • Omaha, NE 68130-1770 • Telephone 402.938.7000 • Fax 402.938.7099 • www.sergeants.com

October 10, 2007

George LaRocca, PM 13
U.S. Environmental Protection Agency
Office of Pesticide Program (7504 P)
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Subject: Gold Seal Certificates

Dear Mr. LaRocca:

Following is a list of products that we would like to receive Gold Seal Certificates. I have enclosed printed labels as well for each of the products listed.

EPA No. 2517-80 **Sergeant's Cyphenothrin + IGR Squeeze-On for Dog**
Product labels:
Sergeant's Gold Flea and Tick Squeeze-On for Dogs
SENTRYPRO XFC Flea and Tick Squeeze-On for Dogs

George has Jacket

EPA No. 2517-85 **Sergeant's Cyphenothrin Squeeze-On for Dogs**
Product label:
Sergeant's Silver Flea and Tick Squeeze-On for Dogs

EPA No. 2517-87 **MarketQuest One-Drop Flea & Tick Control with Nylar ® Insect Growth Regulator**
Product label:
Sergeant's SENTRY PRO Squeeze-On Flea and Tick Control for Dogs

EPA No. 69332-3-2517 **SPI# 8208-55D**
Product labels:
Sergeant's Gold Squeeze-On for Cats & Kittens
Sentry PurrScriptions plus Squeeze-On for cats and kittens

EPA No. 69332-4-2517 **PL #1001**
Product labels:
Sergeant's Silver Flea and Tick Squeeze-On for Cats and Kittens
SENTRY PurrScriptions Squeeze-On for Cats and Kittens

Should you have further questions, please do not hesitate to ask.

Best Regards,

Susan Kane

Susan Kane
Regulatory Coordinator
Sergeant's Pet Care Products, Inc.
Skane@sergeants.com
(402) 938-7065

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

October t5, 2007

I, George Larocca, Insecticide Branch, Registration Division, Office of Pesticide Programs, Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency ("EPA"), certify that the pesticide product (s) listed below is, as of the date of this letter, a registered product under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, and that as such, the product(s) may be sold and marketed in the United States of America as authorized and limited by FIFRA. A true and correct copy of the product label approved by EPA is attached to accompany this letter.

Registration of this product(s) with EPA also denotes that the registrant listed below is responsible for ensuring full compilance with all the laws of the United States of America, or governing jurisdiction, regarding the sale, storage and/or disposal of the product(s). Further, the recipient of this letter is on notice that the referenced registration and/or the accompanying label may change subsequent to the date of this letter. EPA assumes no responsibility to notify the recipient(s) of this letter of any change in the status of the registration(s) and/or the product label for the product(s) listed below.

EPA has Issued registration numbers for the product(s) listed below to:

Sergeant's Pet Care Products, Inc.
509 Tower Valley Drive
Hilisboro, MO 63050

EPA Registration Number: 2517-85
Name of Product: SERGEANT'S CYPHENOTHRIN SQUEEZE-ON FOR DOGS

George Larocca
Risk Manager t3
Insecticide Branch
Registration Division (7505P)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C 20460

NOTIFICATION

APR 04 2007

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Carrie Daniels
Representative of Sergeant's Pet Care Products, Inc.
Exponent™
1730 Rhode Island Ave., NW – Suite 1100
Washington, DC 20036

APR 4 2007

SUBJECT: Application for Pesticide Notification
Sergeant's Cyphenothrin Squeeze-On for Dogs
EPA Reg. No. 2517-85
Application Dated January 17, 2007

Dear Ms. Daniels:

The Agency is in receipt of your Application for Pesticide Notification under Pesticide Registration Notice (PRN) 98-10 for the product above. The Registration Division (RD) has conducted a review of this request for its applicability under PRN 98-10 and finds that the actions requested fall within the scope of PRN 98-10. The label submitted with the application has been stamped "Notification" and will be placed in our records.

If you have any questions, please me directly at 703-305-6249 or Terri Stowe of my staff at 703-305-6117.

Sincerely,

Linda Arrington
Notifications & Minor Formulations Team Leader
Registration Division (7505P)
Office of Pesticide Programs

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060

United States
Environmental Protection Agency
Washington, DC 20460

- [ ] Registration
- [ ] Amendment
- [X] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
2517-85	George LaRocca	[X] None [ ] Restricted
4. Company/Product (Name)	**PM#**	
Sergeant's Cyphenothrin Squeeze-On for Dogs	13	

5. Name and Address of Applicant *(Include ZIP Code)*

Sergeant's Pet Care Products, Inc.
2625 South 158 Plaza
Omaha, NE 68130

[ ] *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3(b)(i, my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section - II

- [ ] Amendment - Explain below.
- [ ] Resubmission in response to Agency letter dated _____
- [X] Notification - Explain below.
- [ ] Final printed labels in repsonse to Agency letter dated _____
- [ ] "Me Too" Application.
- [ ] Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Submission of an Notification pursuant to PR Notice 98-10.

NOTIFICATION

APR 04 2007

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify) _____
* ***Certification must be submitted***	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
[ ] Label [ ] Container		[ ]

6. Manner in Which Label is Affixed to Product [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Carrie Daniels	Authorized Representative	202-772-4916

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowlingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title	
[signature]	Authorized Representative	
4. Typed Name	**5. Date**	
Carrie Daniels	1/17/07	

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

[MASTER CARTON/PACK LABEL-FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On for Dogs

NOTIFICATION

APR 0 4 2007

[ABN : Sergeant's Silver Flea and Tick Squeeze-On for Dogs]
[ABN: Sergeant's Silver Squeeze-On for Dogs]
[ABN: Sentry XFC Squeeze-On for Dogs]
[ABN: Sentry XFC Flea and Tick Squeeze-On for Dogs]

- DO NOT USE ON CATS [Box/Icon with cat image and cross-out]
- [Flea & Tick control for dogs and puppies over 12 weeks of age]
- [Three in one protection [Kills fleas, ticks and mosquitoes]
- [[Three] [3] Way Protection [Kills fleas, ticks and mosquitoes]
- [Three in one protection! Kills fleas, ticks and mosquitoes]
- [Up to 4 week Flea and Tick Treatment]
- [Up to 4 week Flea and Tick Control][4 week [monthly] protection]
- [Monthly flea and tick control]
- [For dogs & puppies (over 12 weeks of age) More than 9 lbs.]
- [For dogs & puppies (over 12 weeks of age) 9 to 20 lbs]
- [For dogs & puppies (over 12 weeks of age) 21 to 39 lbs]
- [For dogs & puppies (over 12 weeks of age) 40 to 60 lbs]
- [For dogs & puppies (over 12 weeks of age) 61 lbs and over]
- [Three applications (for cartons with 3 applications)] and/or [3 month supply] or [12 week supply]
- [For dogs [9 lbs and up] or [9 lbs to 20 lbs] or [21 lbs to 39 lbs] or [40 lbs to 60 lbs] or [61 lbs and over]
- [Best if used year round!]
- [Kills & Repels fleas up to [4 weeks]!]
- Kills [& repels] fleas in as little as 1 hour!]
- Kills [& repels] ticks in as little as 3 hours!]
- [Kills & Repels ticks for up to [4 weeks]!]
- [Kills & Repels deer ticks (vector of lyme disease) for up to 4 weeks!]
- [Kills & Repels ticks (including deer ticks) for up to 4 weeks!)
- [Kills & Repels brown dog ticks [(*Rhipicephalus sanguineus*)] for up to 4 weeks!]
- [Kills & Repels American dog ticks [(*Dermacentor variabilis*)] for up to 4 weeks!]
- [Apply every [4 weeks]!][1 month]
- [Up to 4 weeks of flea & tick treatment!]
- [Kills [& Repels] fleas and ticks for up to 4 weeks!]
- [Kills [and Repels] mosquitoes]
- [Dogs can be bathed 24 hours after squeeze-on is applied]
- [Reapply once every 4 weeks.] [Reapply monthly]

- [May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[NOTE: Text or images in [ ] on this label denotes optional statements and/or images that may be used on front, back, sides, top or bottom of carton/pack and/or tube label panels.]

ACTIVE INGEDIENTS:
Cyphenothrin (CAS # 39515-40-7).....40.0%
OTHER INGREDIENTS:.....60.0%
TOTAL:.....100.0%

[NOTE: Due to limited size of carton/pack labeling, the "Ingredient Statement" may be placed to "prominently" appear on the Back Carton/Pack label panel]

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [back] [or] [side] ~~label~~ panel[s] for additional precautionary statements

NET CONTENTS: [Three] [Six] [Twelve] 1.5 ml (0.05 fl. oz.) tubes, or
[Three] [Six] [Twelve] 3.0 ml (0.10 fl. oz.) tubes, or
[Three] [Six] [Twelve] 4.5 ml (0.15 fl. oz.) tubes, or
[Three] [Six] [Twelve] 6.0 ml (0.20 fl. oz.) tubes

[MASTER CARTON/PACK LABEL – BACK/SIDE PANELS]

Sergeant's Cyphenothrin
Squeeze-On for Dogs

NOTIFICATION

APR 04 2007

[DO NOT USE ON CATS] [Box/icon with cat image and cross-out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Harmful if swallowed or absorbed through skin. Wash thoroughly with soap and water after handling.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.
HOTLINE NUMBER Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS-1-800-781-4738 for emergency medical treatment information.	
NOTE TO PHYSICIAN OR VETERINARIAN Treat patient symptomatically	

DIRECTIONS FOR USE
It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, [snap or] cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 9 lbs. to 20 lbs.: [For cartons containing 1.5 ml (0.05 fl. oz.) applicator tubes] Apply one tube (1.5 ml) (0.05 fl. oz.) [as a spot or stripe to the dog's back between the shoulder blades.] or [from the back of the neck to a point midway between the neck and tail.]

For Dogs Weighing 21 lbs. to 39 lbs.: [For cartons containing two 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) [as a spot or stripe to the dog's back between the shoulder blades.] or [from the back of the neck to a point midway between the neck and tail.]] [For cartons containing one 3.0 ml (0.10 fl. oz.) applicator tube] [Apply one tube (3.0 ml) (0.10 fl. oz.) [as a spot or stripe to the dog's back between the shoulder blades.] or [from the back of the neck to a point midway between the neck and tail.]]

For Dogs Weighing 40 lbs. to 60 lbs.: [For cartons containing three 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades and apply the third tube from the back of the neck to a point midway between the neck and tail.] [For cartons containing one tube (4.5 ml) (0.15 fl. oz.)] [Apply one tube (4.5 ml) (0.15 fl. oz.) from the back of the neck to a point midway between the neck and tail.]

For Dogs Weighing 61 lbs. and Over [For cartons containing at least four 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml) (0.05 fl. oz.) from the back of the neck to a point midway between the neck and tail.] or [For cartons containing at least two 3.0 ml (0.10 fl. oz.) applicator tubes] [Apply one tube (3.0 ml) (0.10 fl. oz.) as a spot or strip to the dog's back between the shoulder blades and apply the contents of the other tube (3.0 ml) (0.10 fl. oz.) from the back of the neck

to a point midway between the neck and tail.] [For cartons containing one tube (6.0 ml) (0.20 fl. oz.)] [Apply one tube (6.0 ml) (0.20 fl. oz.) [as a spot or stripe to the dog's back between the shoulder blades.] or [from the back of the neck to a point midway between the neck and tail.]]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Do not remove tube from the pack until ready to use. Store in a cool (below 25° C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

Pesticide Disposal: If empty: do not reuse this container. Place in trash or offer for recycling if available. If partially filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On for Dogs is an effective and easy to use product.][As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On for Dogs should be used as part of a [an overall] [complete] program [aimed at][to][intended to][reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]
Visit us at www.sergeants.com

Made in the USA

[Sergeant's is committed to providing high quality products. If you have any questions or comments about this product, please write: Sergeant's Consumer Response: P.O. Box 540399, Omaha, NE 68154-0399.]

[In case of an emergency: call 1-800-781-4738.]
[Non-emergency: call 1-800-224-PETS (7387)]

[WARRANTY: SERGEANT'S PET CARE, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENT MADE ON THIS LABEL.]

[Made in the USA For:] or [Manufactured by:]
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703

[BAR CODE AREA]

EPA Reg. No. 2517-85
EPA Est. No.

[MASTER LABEL-TUBE/APPLICATOR LABEL]

PANELS-

Sergeant's Cyphenothrin Squeeze-On for Dogs, [Box/Icon with cat image and cross-out], [1.5 ml] [0.05 fl. oz.] or [3.0 ml] [0.10 fl. oz.] or [4.5 ml] [0.15 fl. oz.] or [6.0 ml] [0.20 fl. oz.], Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN, EPA REG. NO. 2517-85 [Box/Icon with cat image and cross-out]

Exponent

Exponent
1730 Rhode Island Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

NOTIFICATION

APR 04 2007

January 17, 2007

Sherada Hobgood
U.S. Environmental Protection Agency (NOTIF)
Office of Pesticide Program (7504 P)
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Subject: Label Notification
Sergeant's Cyphenothrin Squeeze-On for Dogs
EPA Registration Number 2517-85
Project No. WD00758.000

Dear Ms. Hobgood:

On behalf of our client, Sergeant's Pet Care Products, Inc. (EPA Company Number 2517), Exponent is submitting a notification for a revised label for the product Sergeant's Cyphenothrin Squeeze-On for Dogs (EPA Registration Number 2517-85), containing the registered active ingredient cyphenothrin. Please find the following information enclosed in support of this notification:

- EPA Form 8570-1
- Product label (5 copies)

The enclosed label has been revised to correct several typographical errors. Additionally, the application instruction "from the back of the neck to a point midway between the neck and tail" has been added as an application instruction option in each weight range. This language was required be EPA in the instructions for the 40 lbs to 60 lbs, and 61 lbs. and over weight ranges. This change will provide consistency in the application instructions between all of the weight ranges. A copy of the label with all changes highlighted is enclosed.

This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula of this product. I understand that it is a violation of 18 U.S.C. Sec. 1001 to willfully make any false statement to EPA. I further understand that

if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be subject to enforcement action and penalties under sections 12 and 14 of FIFRA.

If you have any questions, please contact me at (202) 772-4916.

Sincerely,

Carrie Daniels
Authorized Representative of
Sergeant's Pet Care Products, Inc.

Enclosures

cc: George LaRocca, EPA
Susan Kane, Sergeant's
Larry Nouvel, Nouvel
Jim Messina, Exponent

3 4 2 2

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 9 2007

Ms. Sherri Gray
Authorized Representative
Sergeant's Pet Care Products, Inc.
2625 South 158th Plaza
Omaha, NE 68130

RE: Label Revisions
EPA Reg. No.: 2517-85
Date Submitted: January 3, 2007

Dear Ms. Gray:

The Agency is in receipt of your Application for Pesticide Notification under Pesticide Registration Notice (PRN) 98-10 dated January 3, 2007, for the product Sergeant's Cyphenothrin Squeeze-On for Dogs. The Registration Division (RD) has conducted a review of this request for its applicability under PRN 98-10 and finds that the action(s) requested fall within the scope of PRN 98-10. The label submitted with the application has been stamped "Notification" and will be placed in our records.

If you have any questions, please call me directly at 703-305-6249 or Joyce Edwards of my staff at 703-305-5479.

Sincerely,

Linda Arrington
Notifications & Minor Formulations Team Leader
Registration Division (7505P)
Office of Pesticide Programs

Please read instructions on reverse before completing

Form Approved. OMB No. 2070-0060

United States
Environmental Protection Agency
Washington, DC 20460

[ ] Registration
[ ] Amendment
[X] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
2517-85	George LaRocca	[X] None [ ] Restricted
4. Company/Product (Name)	**PM#**	
Sergeant's Cyphenothrin Squeeze-On for Dogs	13	

5. Name and Address of Applicant *(Include ZIP Code)*

Sergeant's Pet Care Products, Inc.
2625 South 158 Plaza
Omaha, NE 68130

[ ] *Check if this is a new address*

6. Expedited Reveiw. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section - II

[ ] Amendment - Explain below.
[ ] Resubmission in response to Agency letter dated _____
[X] Notification - Explain below.
[ ] Final printed labels in repsonse to Agency letter dated _____
[ ] "Me Too" Application.
[ ] Other - Explain below.

NOTIFICATION
MAR 9 2007

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Submission of label revisions pursuant to PR Notice 98-10.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify) _____
* *Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
[ ] Label [ ] Container		[ ]

6. Manner in Which Label is Affixed to Product: [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Sherri Gray	Authorized Representative	202-772-4904

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowlingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title
Sherri Gray	Authorized Representative
4. Typed Name	**5. Date**
Sherri Gray	1/31/07

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

[MASTER CARTON/PACK LABEL-FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On for Dogs

[ABN : Sergeant's Silver Flea and Tick Squeeze-On for Dogs]
[ABN: Sergeant's Silver Squeeze-On for Dogs]
[ABN: Sentry XFC Squeeze-On for Dogs]
[ABN: Sentry XFC Flea and Tick Squeeze-On for Dogs]

- DO NOT USE ON CATS [Box/Icon with cat image and cross-out]
- [Flea & Tick control for dogs and puppies over 12 weeks of age]
- [Three in one protection [Kills fleas, ticks and mosquitoes]
- [[Three] [3] Way Protection [Kills fleas, ticks and mosquitoes]
- [Three in one protection! Kills fleas, ticks and mosquitoes]
- [Up to 4 week Flea and Tick Treatment]
- [Up to 4 week Flea and Tick Control][4 week [monthly] protection]
- [Monthly flea and tick control]
- [For dogs & puppies (over 12 weeks of age) More than 9 lbs.]
- [For dogs & puppies (over 12 weeks of age) 9 to 20 lbs]
- [For dogs & puppies (over 12 weeks of age) 21 to 39 lbs]
- [For dogs & puppies (over 12 weeks of age) 40 to 60 lbs]
- [For dogs & puppies (over 12 weeks of age) 61 lbs and over]
- [Three applications (for cartons with 3 applications)] and/or [3 month supply] or [12 week supply]
- [For dogs [9 lbs and up] or [9 lbs to 20 lbs] or [21 lbs to 39 lbs] or [40 lbs to 60 lbs] or [61 lbs and over]
- [Best if used year round!]
- [Kills & Repels fleas up to [4 weeks]!]
- Kills [& repels] fleas in as little as 1 hour!]
- Kills [& repels] ticks in as little as 3 hours!]
- [Kills & Repels ticks for up to [4 weeks]!]
- [Kills & Repels deer ticks (vector of lyme disease) for up to 4 weeks!]
- [Kills & Repels ticks (including deer ticks) for up to 4 weeks!)
- [Kills & Repels brown dog ticks [(*Rhipicephalus sanguineus*)] for up to 4 weeks!]
- [Kills & Repels American dog ticks [(*Dermacentor variabilis*)] for up to 4 weeks!]
- [Apply every [4 weeks]!][1 month]
- [Up to 4 weeks of flea & tick treatment!]
- [Kills [& Repels] fleas and ticks for up to 4 weeks!]
- [Kills [and Repels] mosquitoes]
- [Dogs can be bathed 24 hours after squeeze-on is applied]
- [Reapply once every 4 weeks.] [Reapply monthly]

- [May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[NOTE: Text or images in [ ] on this label denotes optional statements and/or images that may be used on front, back, sides, top or bottom of carton/pack and/or tube label panels.]

ACTIVE INGEDIENT:
Cyphenothrin (CAS # 39515-40-7).....40.0%
OTHER INGREDIENTS:.....60.0%
TOTAL:.....100.0%

[NOTE: Due to limited size of carton/pack labeling, the "Ingredient Statement" may be placed to "prominently" appear on the Back Carton/Pack label panel]

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [back] [or] [side] label panel[s] for additional precautionary statements

NET CONTENTS: [Three] [Six] [Twelve] 1.5 ml (0.05 fl. oz.) tubes, or
[Three] [Six] [Twelve] 3.0 ml (0.10 fl. oz.) tubes, or
[Three] [Six] [Twelve] 4.5 ml (0.15 fl. oz.) tubes, or
[Three] [Six] [Twelve] 6.0 ml (0.20 fl. oz.) tubes

[MASTER CARTON/PACK LABEL – BACK/SIDE PANELS]

Sergeant's Cyphenothrin
Squeeze-On for Dogs

[DO NOT USE ON CATS] [Box/icon with cat image and cross-out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Harmful if swallowed or absorbed through skin. Wash thoroughly with soap and water after handling.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.
HOTLINE NUMBER Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-781-4738 for emergency medical treatment information.	
NOTE TO PHYSICIAN OR VETERINARIAN Treat patient symptomatically	

DIRECTIONS FOR USE
It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, [snap or] cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 9 lbs. to 20 lbs.: [For cartons containing 1.5 ml (0.05 fl. oz.) applicator tubes] Apply one tube (1.5 ml)(0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.

For Dogs Weighing 21 lbs. to 39 lbs.: [For cartons containing two 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml)(0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.] [For cartons containing one 3.0 ml (0.10 fl. oz.) applicator tube] [Apply one tube (3.0 ml)(0.10 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.]

For Dogs Weighing 40 lbs. to 60 lbs.: [For cartons containing three 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades and apply the third tube from the back of the neck to a point midway between the neck and tail.] [For cartons containing one tube (4.5 ml) (0.15 fl. oz.)] [Apply one tube (4.5 ml) (0.15 fl. oz.) from the back of the neck to a point midway between the neck and tail.]

For Dogs Weighing 61 lbs. and Over [For cartons containing at least four 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml) (0.05 fl. oz.) from the back of the neck to a point midway between the neck and tail.] or [For cartons containing at least two 3.0 ml (0.10 fl. oz.) applicator tubes] [Apply one tube (3.0 ml) (0.10 fl. oz.) as a spot or strip to the dog's back between the shoulder blades and apply the contents of the other tube (3.0 ml) (0.10 fl. oz.) from the back of the neck to a point midway between the neck and tail.] [For cartons containing one tube (6.0 ml)

(0.20 fl. oz.)] [Apply one tube (6.0 ml) (0.20 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.
Pesticide Storage: Do not remove tube from the pack until ready to use. Store in a cool (below 25° C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.
Pesticide Disposal: If empty: do not reuse this container. Place in trash or offer for recycling if available. If partially filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On for Dogs is an effective and easy to use product.][As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On for Dogs should be used as part of a [an overall] [complete] program [aimed at][to][intended to][reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]
Visit us at: www.sergeants.com

Made in the USA

[Sergeant's is committed to providing high quality products. If you have any questions or comments about this product, please write: Sergeant's Consumer Response: P.O. Box 540399, Omaha, NE 68154-0399.]

[In case of emergency, call 1-800-781-4738.]
[Non-emergency, call 1-800-224-PETS]

[WARRANTY: SERGEANT'S PET CARE, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENT MADE ON THIS LABEL.]

Manufactured by:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703

[BAR CODE AREA]

EPA Reg. No. 2517-85
EPA Est. No.

[MASTER LABEL-TUBE/APPLICATOR LABEL]

PANELS-

Sergeant's Cyphenothrin Squeeze-On for Dogs, [Box/Icon with cat image and cross-out], [1.5 ml] [0.05 fl. oz.] or [3.0 ml] [0.10 fl. oz.] or [4.5 ml] [0.15 fl. oz.] or [6.0 ml] [0.20 fl. oz.], Active Ingredient: Cyphenothrin 40.0% W/W;

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN, EPA REG. NO. 2517-85

Exponent

Exponent
1730 Rhode Island Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

January 3, 2007

Sherada Hobgood
U.S. Environmental Protection Agency (NOTIF)
Office of Pesticide Program (7504 P)
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Subject: Label Notification
Sergeant's Cyphenothrin Squeeze-On for Dogs
EPA Registration Number 2517-85
Project No. WD00758.000

Dear Ms. Hobgood:

On behalf of our client, Sergeant's Pet Care Products, Inc. (EPA Company Number 2517), Exponent is submitting a notification for a revised label for the product Sergeant's Cyphenothrin Squeeze-On for Dogs (EPA Registration Number 2517-85), containing the registered active ingredient cyphenothrin. Please find the following information enclosed in support of this notification:

- EPA Form 8570-1
- Product label (5 copies)

The enclosed label has been updated to clarify a few minor changes. A copy of the label with all changes highlighted is enclosed.

This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula of this product. I understand that it is a violation of 18 U.S.C. Sec. 1001 to willfully make any false statement to EPA. I further understand that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be subject to enforcement action and penalties under sections 12 and 14 of FIFRA.

If you have any questions, please contact me at (202) 772-4964.

Sincerely,

Sherri Gray
Authorized Representative of
Sergeant's Pet Care Products, Inc.

Enclosures

cc: George LaRocca, EPA
Susan Kane, Sergeant's
Larry Nouvel, Nouvel
Jim Messina, Exponent

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

01/11/2007

MEMORANDUM

SUBJECT: Cyphenothrin: Response to Sergeant's Pet Products, Inc. Comments on HED's Review of the Draft Protocol (D330741), "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation:" DP Barcode: 333535, PC Code: 129013

FROM: Wade Britton, MPH, Risk Assessor/ Industrial Hygienist
Reregistration Branch 3
Health Effects Division (7509P)

THROUGH: Christina Swartz, Branch Chief
Registration Branch 2
Health Effects Division (7509P)

TO: George LaRocca and Linda DeLuise
Insecticides Branch
Registration Division (RD) (7505P)

This document serves as a response to Sergeant's Pet Products, Inc. comments on "Cyphenothrin: Review of Sergeant's Pet Products, Inc. Draft Protocol, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation (D330741, 09/21/06)" A memo was submitted by Exponent, on behalf of Sergeant's Pet Products, Inc. confirming that the registrant plans to conduct a cyphenothrin-specific dislodgeability study according to EPA's revised protocol upon receiving final feedback from the Agency in reference to the submitted comments. In particular, the registrant requested that the Agency provide further explanation for differences observed between the Agency's draft dislodgeability study protocol for pet spot-on products and previous protocol requirements. This memo provides responses to the following comments.

Comment1. EPA has amended the protocol to require application via syringe, rather than from the final package in which the product will be distributed, as was previously required. To maximize flexibility for the registrant, Sergeant's requests that the Agency allow application via either final packaging or a syringe as appropriate.

Re: HED concurs. The amended protocol referenced in HED's response to the registrant (D330741) was derived from a draft dislodgeability protocol for pet spot-on products composed by HED. It was altered slightly to be specific for Sergeant's pet spot-on study. The current general draft protocol allows for application by either final packaging or by syringe.

Comment2. The addition of the pilot/preliminary 5 dog study and the "hand to mouth" component to the experimental study significantly increase the number of animals required, but the scientific benefit of these components, if any, may not be worth the extra cost. Typical EPA pet animal protocols require a minimum of 6 subjects per test group. However, with the "pet hug" and "hand to mouth" scenarios, a total of 20 dogs will be used. Furthermore, the additional cost of the 25 required laboratory-bred Beagles is prohibitive for a study of this nature.

Re: As described in EPA's review of Sergeant's pet protocol (D330741), the Agency determined that the pilot study "should reduce the number of replicates required for each time interval, while producing results representative of exposure to residues on the pet." The study director should make use of the pilot study to determine the point at which saturation occurs, or where increasing the number of replicates does not provide additional information. This should increase the potential for useful data to be derived from the experimental portion of the study by limiting the possibility of non-detects or the need for additional, unnecessary samples beyond saturation.

HED concurs that while the addition of the "hand to mouth" component to the draft dislodgeability protocol for pet spot-on studies could be useful to explore this once daily event, it may be costly for the registrant. The Agency can make use of the "pet hug" data derived from the dislodgeability study (pilot and experimental studies) and extrapolate these data for application to any assessed "hand to mouth" scenarios.

Comment 3. The protocol for the pilot/ preliminary 5 dog study does not provide sufficient detail to ensure that the determination of the study director regarding the procedures for the field portion of the study will be acceptable to the Agency upon review. The decision appears to be subjective; therefore, we request that the Agency provide clearer guidance. Specifically, EPA should articulate the criterion by which the appropriate number of stroking simulations to be performed will be determined.

Re: As described in EPA's review of Sergeant's pet protocol (D330741), the Agency recommends that, "it will be the duty of the study director to determine what number of petting simulations is necessary to load the sampling media, or at which point increasing the number of replicates provide no additional information." To that end, the decision will be subjective, as it relies upon the judgment and expertise of the study director. If the registrant deems necessary, results and conclusions of the preliminary study (pilot)

can be reviewed by the Agency prior to the administration of the experimental study or a conference call or meeting could be held to discuss preliminary results.

The draft dislodgeability protocol was conceived for the purpose of harmonizing and improving the quality of the study data submitted for pet spot-on products. It is intended to be interpreted as a guidance document for the execution of the dislodgeability studies. The Agency is aware that interpretation of the draft protocol may vary widely and such factors will be taken into account when results are submitted for review; however, the Agency cannot control all factors which pertain to each study (e.g., data quality) and, therefore, cannot ensure that results will be usable for risk assessment purposes.

Comment 4. In the hand to mouth portion of the experimental study added by the Agency, the protocol indicates that sampling may be discontinued if and when two non-detect samples are identified from the results of all glove samples for a given time period analysis. However, for this portion of the study there is only one petting simulation that takes place at 24 hours after the application of the product to the dogs. Therefore, the discontinuance statements should be omitted from the protocol for the hand to mouth component.

Re: HED concurs. A pilot/ preliminary study should not be required for the "hand to mouth" portion of the pet spot-on, and HED is not requiring Sergeant's to perform this portion of the study. The general draft protocol (not specific to Sergeant's study) will be corrected to specify that the pilot/ preliminary study will not include simulations for the "hand to mouth" portion. The pilot study will still be required for the "pet hug" portion of the pet spot-on study.

Comment5. EPA states that the second cotton glove will be used to determine if breakthrough is occurring and that analysis of the nitrile glove will be required only when breakthrough is observed. EPA should clarify how the analytical results from the various gloves will be "combined" (as indicated in A.9). Will ½ the LOQ or LOD be added for all non-quantifiable or non-detectable residues from all three glove layers? This could be exceedingly conservative in some cases. EPA should clarify how glove analyses will be combined and analyzed.

Re: If results of the pilot study dictate that the 2 cotton glove layers and the Nitrile glove layer are necessary, then the Agency will combine the resulting residue for all three layers. ½ the LOQ/ LOD will be added for all non-quantifiable or non-detectable residues for each glove layer required. HED recognizes the conservatism of this approach and, if risks of concern were to result, the Agency would potentially characterize the resulting risks as such. In addition, the Agency is willing to discuss other options when the data are available.

Comment 6. Finally, Sergeant's wishes to raise the issue of terminology. In the protocol provided, the words "simulation" and "replicates" are used interchangeably and also in distinct fashions. Sergeant's suggests that the word "replicate" be associated with the number of dogs (i.e., data gathered from 10 dogs will constitute 10 replicates) and that the term "stroking procedure" be introduced, such that a "simulation" will consist of X

stroking procedures (where X is determined in the pilot study and the stroking procedure is defined as in the current protocol). Sergeant's believes that these or similar changes in the terminology will improve the protocol.

Re: HED concurs. Draft protocol language will be altered to adopt the recommendation. Please reflect recommended changes in the language drafted for the pet spot-on study.

Comment7. Based on discussion with Agency personnel, Sergeant's understanding is that the use of the latex glove under the cotton glove removes the dislodgeability study from consideration of the human testing review board. Please provide confirmation if this is the Agency's understanding as well.

Re: The Agency is currently debating this topic and many more in reference to the draft study protocol for the dislodgeability pet spot-on products. It is the intention of HED to submit the draft protocol to be reviewed by the human testing review board.

Comment 8. In addition to the above comments specific to the use of this protocol to support Sergeant's pending registration, Sergeant's would like to add a general comment regarding this protocol as it may be used for other registrants or future Sergeant's products. While it seems intuitive that the transferable fraction measured for the "pet hug" and "hand to mouth" scenarios will be different (due to the likely less intensive contact associated with the hand to mouth scenario), one avenue to reduce the costs of this study would be to allow registrants to conduct only the hug scenario. Sergeant's suggests that the protocol include the flexibility for registrants to decide whether to generate specific data for just the hug scenario or for both the hug and hand to mouth scenario.

Re: HED concurs. While the addition of the "hand to mouth" component to the draft protocol could be useful to explore this once daily event, it may be costly for the registrant. The Agency can make use of the "pet hug" data derived from the dislodgeability study and extrapolate these data for application to any assessed "hand to mouth" scenarios. HED recommends that the registrant move forward with the study disregarding the stroking procedure specific to the "hand to mouth" portion of the draft protocol.

1-26-07

Exponent

Exponent
1730 Rhode Island Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
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January 25, 2007

George LaRocca
U.S. Environmental Protection Agency
Office of Pesticide Program (7504 P)
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Subject: Sergeant's Cyphenothrin Squeeze-On for Dogs
EPA Registration Number 2517-85

Dear Mr. LaRocca:

On behalf of our client, Sergeant's Pet Care Products, Inc. (EPA Company Number 2517), Exponent is submitting the final printed label for the product Sergeant's Cyphenothrin Squeeze-On for Dogs (EPA Registration Number 2517-85), containing the registered active ingredient cyphenothrin. Please find the following information enclosed:

- EPA Form 8570-1
- Product label (3 copies)

The enclosed label has been revised to reflect the changes required in the Stamped Approved Label dated November 22, 2006. If you have any questions, please contact me at (202) 772-4916.

NOT REVIEWED
In Accordance with PR Notice 82 2
Based On Draft Labeling Dated 82 2

Sincerely,

Carrie Daniels
Authorized Representative of
Sergeant's Pet Care Products, Inc.

Enclosures

cc: Susan Kane, Sergeant's
Larry Nouvel, Nouvel
Jim Messina, Exponent

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060

United States
Environmental Protection Agency
Washington, DC 20460

[ ] Registration
[ ] Amendment
[X] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
2517-85	George LaRocca	[X] None [ ] Restricted
4. Company/Product (Name)	**PM#**	
Sergeant's Cyphenothrin Squeeze-On for Dogs	13	

5. Name and Address of Applicant *(Include ZIP Code)*

Sergeant's Pet Care Products, Inc.
2637 South 158 Plaza
Omaha, NE 68130

[ ] *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section - II

[ ] Amendment - Explain below.
[ ] Resubmission in response to Agency letter dated _____
[ ] Notification - Explain below.
[X] Final printed labels in response to Agency letter dated November 22, 2006
[ ] "Me Too" Application.
[ ] Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Submission of a Final Printed Label

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify)
* ***Certification must be submitted***	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Site(s) Retail Container	5. Location of Label Directions
[ ] Label [ ] Container		[ ]

6. Manner in Which Label is Affixed to Product [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Carrie Daniels	Authorized Representative	202-772-4916

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title	4. Typed Name	5. Date
Carrie Daniels	Authorized Representative	Carrie Daniels	1/25/07

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

[MASTER CARTON/PACK LABEL-FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On for Dogs

[ABN : Sergeant's Silver Flea and Tick Squeeze-On for Dogs]
[ABN: Sergeant's Silver Squeeze-On for Dogs]
[ABN: Sentry XFC Squeeze-On for Dogs]
[ABN: Sentry XFC Flea and Tick Squeeze-On for Dogs]

- DO NOT USE ON CATS [Box/Icon with cat image and cross-out]
- ~~[Pleasant fresh scent [or] Fragrance [or] "a specific fragrance(s) will be identified"]~~
- [Flea & Tick control for dogs and puppies over 12 weeks of age]
- [Three in one protection [Kills fleas, ticks and mosquitoes]
- [[Three] [3] Way Protection [Kills fleas, ticks and mosquitoes]
- [Three in one protection! Kills fleas, ticks and mosquitoes]
- [Up to 4 week Flea and Tick Treatment]
- [Up to 4 week Flea and Tick Control][4 week [monthly] protection]
- [Monthly flea and tick control]
- [For dogs & puppies (over 12 weeks of age) More than 9 lbs.]
- [For dogs & puppies (over 12 weeks of age) 9 to 20 lbs]
- [For dogs & puppies (over 12 weeks of age) 21 to 39 lbs]
- [For dogs & puppies (over 12 weeks of age) 40 to 60 lbs]
- [For dogs & puppies (over 12 weeks of age) 61 lbs and over]
- [Three applications (for cartons with 3 applications)] and/or [3 month supply] or [12 week supply]
- [For dogs [9 lbs and up] or [9 lbs to 20 lbs] or [21 lbs to 39 lbs] or [40 lbs to 60 lbs] or [61 lbs and over]
- [Best if used year round!]
- [Kills & Repels fleas up to [4 weeks]!]
- Kills [& repels] fleas in as little as 1 hour!]
- Kills [& repels] ticks in as little as 3 hours!]
- [Kills & Repels ticks for up to [4 weeks]!]
- [Kills & Repels deer ticks (vector of lyme disease) for up to 4 weeks!]
- [Kills & Repels ticks (including deer ticks) for up to 4 weeks!)
- [Kills & Repels brown dog ticks [(*Rhipicephalus sanguineus*)] for up to 4 weeks!]
- [Kills & Repels American dog ticks [(*Dermacentor variabilis*)] for up to 4 weeks!]
- [Apply every [4 weeks]!][1 month]
- [Up to 4 weeks of flea & tick treatment!]
- [Kills [& Repels] fleas and ticks for up to 4 weeks!]
- [Kills [and Repels] mosquitoes]
- ~~Waterproof formula~~

- [Dogs can be bathed 24 hours after squeeze-on is applied]
- [Reapply once every 4 weeks.] [Reapply monthly]
- [May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[NOTE: Text or images in [ ] on this label denotes optional statements and/or images that may be used on front, back, sides, top or bottom of carton/pack and/or tube label panels.]

ACTIVE INGEDIENTS:
Cyphenothrin (CAS # 39515-40-7).....40.0%
OTHER INGREDIENTS:.....60.0%
TOTAL:.....100.0%

[NOTE: Due to limited size of carton/pack labeling, the "Ingredient Statement" may be placed to "prominently" appear on the Back Carton/Pack label panel]

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [back] [or] [side] label panel[s] for additional precautionary statements

NET CONTENTS: [Three] [Six] [Twelve] 1.5 ml (0.05 fl. oz.) tubes, or
[Three] [Six] [Twelve] 3.0 ml (0.10 fl. oz.) tubes, or
[Three] [Six] [Twelve] 4.5 ml (0.15 fl. oz.) tubes, or
[Three] [Six] [Twelve] 6.0 ml (0.20 fl. oz.) tubes

[MASTER CARTON/PACK LABEL – BACK/SIDE PANELS]

Sergeant's Cyphenothrin
Squeeze-On for Dogs

[DO NOT USE ON CATS] [Box/icon with cat image and cross-out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Harmful if swallowed or absorbed through skin. Wash thoroughly with soap and water after handling.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.
HOTLINE NUMBER Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS for emergency medical treatment information.	
NOTE TO PHYSICIAN OR VETERINARIAN Treat patient symptomatically	

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, [snap or] cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 9 lbs. to 20 lbs.: [For cartons containing 1.5 ml (0.05 fl. oz.) applicator tubes] Apply one tube (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.

For Dogs Weighing 21 lbs. to 39 lbs.: [For cartons containing two 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades. [For cartons containing one 3.0 ml (0.10 fl. oz.) applicator tube] [Apply one tube (3.0 ml) (0.10 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.]

For Dogs Weighing 40 lbs. to 60 lbs.: [For cartons containing three 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades and apply the third tube from the back of the neck to a point midway between the neck and tail.] [For cartons containing one tube (4.5 ml) (0.15 fl. oz.)] [Apply one tube (4.5 ml) (0.15 fl. oz.) from the back of the neck to a point midway between the neck and tail.]

For Dogs Weighing 61 lbs. and Over [For cartons containing at least four 1.5 ml (0.05 fl. oz.) applicator tubes] [Apply two tubes (1.5 ml) (0.05 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml) (0.05 fl. oz.) from the back of the neck to a point midway between the neck and tail.] or [For cartons containing at least two 3.0 ml (0.10 fl. oz.) applicator tubes] [Apply one tube (3.0 ml) (0.10 fl. oz.) as a spot or strip to the dog's back between the shoulder blades and apply the contents of the other tube (3.0 ml) (0.10 fl. oz.) from the back of the neck to a point midway between the neck and tail.] [For cartons containing one tube (6.0 ml) (0.20 fl. oz.)] [Apply one tube (6.0 ml) (0.20 fl. oz.) as a spot or stripe to the dog's back between the shoulder blades.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Do not remove tube from the pack until ready to use. Store in a cool (below 25° C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

Pesticide Disposal: If empty: do not reuse this container. Place in trash or offer for recycling if available. If partially filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On for Dogs is an effective and easy to use product.][As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On for Dogs should be used as part of a [an overall] [complete] program [aimed at][to][intended to][reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]
www.sergeants.com

Made in the USA

[Sergeant's is committed to providing high quality products. If you have any questions or comments about this product, please write: Sergeant's Consumer Response: P.O. Box 540399, Omaha, NE 68154-0399.]

[In case of emergency: call 1-800-224-PETS]

[WARRANTY: SERGEANT'S PET CARE, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENT MADE ON THIS LABEL.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703

[BAR CODE AREA]

EPA Reg. No. 2517-85
EPA Est. No.

[MASTER LABEL-TUBE/APPLICATOR LABEL]

PANELS-

Sergeant's Cyphenothrin Squeeze-On for Dogs, [Box/Icon with cat image and cross-out], [1.5 ml] [0.05 fl. oz.] or [3.0 ml] [0.10 fl. oz.] or [4.5 ml] [0.15 fl. oz.] or [6.0 ml] [0.20 fl. oz.], Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN, EPA REG. NO. 2517-85

Material to be added to a Mini-Jacket
(in the case where an e-Jacket exists)

Reg. No. 2517-85

Send to SIG: check box [X]

This material is:

- ☐ New stamped-accepted label
- ☐ New CSF
- ☐ Notification
- ☐ Final Printed Label
- ☒ Other: new registration

Instructions: Attach this notice on top of the material. It must be clipped all together and there should be NO STAPLES in the material. Then give the material with this coversheet to staff in the Information Services Center (Room 230).

Reviewer's Name: _____

Phone: _____ Division: _____

Date: 12/21/06

Current as of Wednesday, March 01 2006

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:
X Registration
___ Reregistration
(Under FIFRA as amended)

EPA Reg. Number: 2517-85	Date of Issuance: NOV 22 2006
Term of Issuance: Conditional	
Name of Pesticide Product: Sergeant's Cypernothrin Squeeze- On for Dogs	

Name and Address of Registrant (include ZIP Code):
Sergeant's Pet Care Products, Inc.
2637 South 158 Plaza, Suite 100
Omaha, NE 68130-1703

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is **conditionally** registered in accordance with FIFRA sec. 3(c)(7)(A)(B)provided that:

1. You will submit and/or cite all data required for registration/reregistration of your product under FIFRA sec. 3(c)(5) when the Agency requires all registrants of similar products to submit such data; and submit acceptable responses required for reregistration of your product under FIFRA section 4.

2. You submit as agreed the data listed below conducted in accordance with 40CFR Part 158 test guidelines or agreed upon protocols:

Title of Study	Guideline Reference Number	Date
Cyphenothrin-specific Dislodgeability Study (dogs)	NA	Within 9 months of acceptance of protocol*
Efficacy Study of a Cyphenothrin Spot-On Against fleas, ticks and Mosquitoes	810-1000,3000, 3300	Protocol submitted within one month of Notice of Registration. Study submitted within 9 months of acceptance of protocol.*

Signature of Approving Official:	Date:
[signature]	November 22, 2006

*You must submit a protocol prior to conducting the efficacy for Agency review and approval. We note that the protocol for Cyphenothrin dislodgeability study is currently under review.

3. You will make the following label changes before you release the product for shipment:

a. Revise the EPA Registration Number to read "EPA Registration Number 2517-85.".

b. Under Directions for Use replace "as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail" with "from the back of the neck to a point midway between the neck and tail". Make the same change to the directions beginning, "as a spot or stripe to the dogs back directly in front…"and "apply the contents of the other tube along the dog's back …".

c. The net contents must be expressed in terms of U.S. liquid units or measurements also. It is recommended that the application rates also include US units of measurement.

ACUTE TOXICITY REVIEW

STUDY	MRID	CATEGORY	CLASSIFICATION
Acute Oral	46166103	III	Acceptable
Acute Dermal	46166104	III	Acceptable
Acute Inhalation		IV	Waived
Eye Irritation	46166105	III	Acceptable
Dermal Irritation	46166106	IV	Acceptable
Dermal Sensitization	46166107	Negative	Acceptable

d. Delete "Pleasant and Fresh Scent or Fragrance" since there is no fragrance in the formulation.

e. Move the paragraph beginning, "For External Use on Dogs Only … etc." and to the directions for use section of the label.

f. Delete "Water Proof formula". No data was submitted to support this claim.

3. You must generate studies corresponding to guidelines 830.6317 (one year storage stability) and 830.6320 (corrosion characteristics). The observations must be3 made at 0, 3, 6, 9, and 12 months intervals. The results must be submitted to the Agency along with and electronic format also.

4. Please submit three (3) copies of your final printed labeling before releasing the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). Your release for shipment of the product bearing amended labeling constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

If you have any questions regarding this action, please contact Linda A. DeLuise of my team at (703) 305-5428.

[MASTER CARTON/PACK LABEL-FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On for Dogs

[**ABN** : Sergeant's Silver Flea and Tick Squeeze-On for Dogs]
[**ABN**: Sergeant's Silver Squeeze-On for Dogs]
[**ABN**: Sentry XFC Squeeze-On for Dogs]
[**ABN:** Sentry XFC Flea and Tick Squeeze-On for Dogs]

- DO NOT USE ON CATS [Box/Icon with cat image and cross-out]
- [Pleasant fresh scent [or] Fragrance [or] "a specific fragrance(s) will be identified"]
- [Flea & Tick control for dogs and puppies over 12 weeks of age]
- [Three in one protection [Kills fleas, ticks and mosquitoes]
- [[Three] [3] Way Protection [Kills fleas, ticks and mosquitoes]
- [Three in one protection! Kills fleas, ticks and mosquitoes]
- [Up to 4 week Flea and Tick Treatment]
- [Up to 4 week Flea and Tick Control][4 week [monthly] protection]
- [Monthly flea and tick control]
- [For dogs & puppies (over 12 weeks of age) More than 9 lbs.]
- [For dogs & puppies (over 12 weeks of age) 9 to 20 lbs]
- [For dogs & puppies (over 12 weeks of age) 21 to 39 lbs]
- [For dogs & puppies (over 12 weeks of age) 40 to 60 lbs]
- [For dogs & puppies (over 12 weeks of age) 61 lbs and over]
- [Three applications (for cartons with 3 applications)] and/or [3 month supply] or [12 week supply]
- [For dogs [9 lbs and up] or [9 lbs to 20 lbs] or [21 lbs to 39 lbs] or [40 lbs to 60 lbs] or [61 lbs and over]
- [Best if used year round!]
- [Kills & Repels fleas up to [4 weeks]!]
- Kills [& repels] fleas in as little as 1 hour!]
- Kills [& repels] ticks in as little as 3 hours!]
- [Kills & Repels ticks for up to [4 weeks]!]
- [Kills & Repels deer ticks (vector of lyme disease) for up to 4 weeks!]
- [Kills & Repels ticks (including deer ticks) for up to 4 weeks!)
- [Kills & Repels brown dog ticks [(*Rhipicephalus sanguineus*)] for up to 4 weeks!]
- [Kills & Repels American dog ticks [(*Dermacentor variabilis*)] for up to 4 weeks!]
- [Apply every [4 weeks]!][1 month]
- [Up to 4 weeks of flea & tick treatment!]
- [Kills [& Repels] fleas and ticks for up to 4 weeks!]
- [Kills [and Repels] mosquitoes]

ACCEPTED
with COMMENTS
In EPA Letter Dated:

NOV 22 2005

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 2517-OS

- [Waterproof formula]
- [Dogs can be bathed 24 hours after squeeze-on is applied]
- [Reapply once every 4 weeks.] [Reapply monthly]
- [May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[NOTE: Text or images in [ ] on this label denotes optional statements and/or images that may be used on front, back, sides, top or bottom of carton/pack and/or tube label panels.]

ACTIVE INGEDIENTS:

Cyphenothrin (CAS # 39515-40-7).....40.0%

OTHER INGREDIENTS:.....60.0%

TOTAL:.....100.0%

[NOTE: Due to limited size of carton/pack labeling, the "Ingredient Statement" may be placed to "prominently" appear on the Back Carton/Pack label panel]

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [back] [or] [side] label panel[s] for additional precautionary statements

NET CONTENTS: [Three] [Six] [Twelve] 1.5 ml tubes, or
[Three] [Six] [Twelve] 3.0 ml tubes, or
[Three] [Six] [Twelve] 4.5 ml tubes, or
[Three] [Six] [Twelve] 6.0 ml tubes

[MASTER CARTON/PACK LABEL – BACK/SIDE PANELS]

Sergeant's **Cyphenothrin**
Squeeze-On for Dogs

[DO NOT USE ON CATS] [Box/icon with cat image and cross-out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling. FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.

HOTLINE NUMBER
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS for emergency medical treatment information.
NOTE TO PHYSICIAN OR VETERINARIAN
Treat patient symptomatically

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, [snap or] cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 9 lbs. to 20 lbs.: [For cartons containing 1.5 ml applicator tubes] Apply one tube (1.5 ml) as a spot or strip to the dog's back between the shoulder blades.

For **Dogs Weighing 21 lbs. to 39 lbs.**: [For cartons containing two 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades.] [For cartons containing one 3.0 ml applicator tube] [Apply one tube (3.0 ml) as a spot or stripe to the dog's back between the shoulder blades.]

For **Dogs Weighing 40 lbs.** to **60 lbs.**: [For cartons containing three 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the third tube as a spot or stripe to the dog's back directly in front of the base of the tail.] [For cartons containing one tube (4.5 ml)] [Apply one tube (4.5 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.]

For Dogs Weighing 61 lbs. and Over [For cartons containing at least four 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml) along the dog's back extending to directly in front of the base of the tail.] or [For cartons containing at lease two 3.0 ml applicator tubes] [Apply one tube (3.0 ml) as a spot or strip to the dog's back between the shoulder blades and apply the contents of the other tube (3.0 ml) along the dog's back extending to directly in front of the base of the tail.] [For cartons containing one tube (6.0 ml)] [Apply one tube (6.0 ml) as a spot or stripe to the dog's back between the shoulder blades.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Do not remove tube from the pack until ready to use. Store in a cool (below 25° C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

Pesticide Disposal: If empty: do not reuse this container. Place in trash or offer for recycling if available. If partially filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On for Dogs is an effective and easy to use product.][As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On for Dogs should be used as part of a [an overall] [complete] program [aimed at][to][intended to][reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

www.sergeants.com

Made in the USA

[Sergeant's is committed to providing high quality products. If you have any questions or comments about this product, please write: Sergeant's Consumer Response: P.O. Box 540399, Omaha, NE 68154-0399.]

[In case of emergency, call 1-800-224-PETS.]

[WARRANTY: SERGEANT'S PET CARE, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENT MADE ON THIS LABEL.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703

[BAR CODE AREA]

EPA Reg. No. 2517-
EPA Est. No.

Label Comments

a. *2517-~~IN~~ Claims*

[MASTER CARTON/PACK LABEL-FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On for Dogs

ABN : Sergeant's Silver Flea and Tick Squeeze-On for Dogs
ABN: Sergeant's Silver Squeeze-On for Dogs
ABN: Sentry XFC Squeeze-On for Dogs
ABN: Sentry XFC Flea and Tick Squeeze-On for Dogs

- DO NOT USE ON CATS [Box/Icon with cat image and cross-out]
- [Pleasant fresh scent [or] Fragrance [or] "a specific fragrance(s) will be identified"]
- [Flea & Tick control for dogs and puppies over 12 weeks of age]
- [Three in one protection [Kills fleas, ticks, and mosquitoes
- [Three Way Protection [Kill fleas, ticks, mosquitoes] [for up to days]
- [Three in one protection! Kills ticks, and
- [Up to 4 week Flea and Tick Treatment]
- [Up to 4 week Flea and Tick Control]
- 4 week [1 month] flea, tick and control
- Monthly flea, tick, and control
- [For dogs & puppies (over 12 weeks of age) More than 9 lbs.]
- [For dogs & puppies (over 12 weeks of age) 9 to 20 lbs]
- [For dogs & puppies (over 12 weeks of age) 21 to 39 lbs]
- [For dogs & puppies (over 12 weeks of age) 40 to 60 lbs]
- [For dogs & puppies (over 12 weeks of age) 61 lbs and over]
- [Three applications (for cartons with 3 applications)] and/or [3 month supply] or [12 week supply]
- [For dogs [9 lbs and up] or [9 lbs to 20 lbs] or [21 lbs to 39 lbs] or [40 lbs to 60 lbs] or [61 lbs and over]
- [Best if used year round!]
- [Kills & Repels fleas up to [4 weeks]!]
- [Kills & Repels ticks for up to [4 weeks]!]
- [Kills & Repels deer ticks (vector of lyme disease) for up to 4 weeks!]
- [Kills & Repels ticks (including deer ticks) for up to 4 weeks!)
- [Kills & Repels brown dog ticks [(*Rhipicephalus sanguineus*)] for up to 4 weeks!]
- [Kills & Repels American dog ticks [(*Dermacentor variabilis*)] for up to 4 weeks!]
- [Apply every [4 weeks]!][1 month]
- [Up to 4 weeks of flea & tick treatment!]
- [Kills & Repels fleas and ticks for up to 4 weeks!]

Comment [MES1]: [28 days][4 weeks]] 1 month] is the conditionally acceptable claim.

Deleted: 30

Comment [MES2]: No acceptable data to support mosquitoes were provided.

Deleted: mosquitoes

Comment [MES3]: No acceptable data to support mosquitoes were provided.

Deleted: mosquito

Comment [MES4]: No acceptable data to support mosquitoes were provided.

Deleted: mosquito

Deleted:

Comment [MES5]: Claims may be included, if they state "Begins to kill & repel..."

Comment [MES6]: No acceptable data to support claims against mosquitoes wereprovided.

Comment [MES7]: No acceptable data to support mosquitoes provided; Dogs have neither been found to be susceptible to WNV nor suitable intermediate hosts resulting in human infection by feeding mosquitoes

Comment [MES8]: No acceptable data to support mosquitoes provided.

Deleted: [Kills & Repels [new[fleas in less than 1 hour!]¶
<#>[Kills & Repels [new] ticks in less than 3 hours![¶

Deleted: [Kills mosquitoes for up to 30 days!]

Deleted: ¶

Deleted: [Kill mosquitoes (vector of West Nile Virus) for up to 30 days!]

Deleted: ¶

Deleted: [Protects against blood feeding by mosquitoes (vector of heartworm) for up to 30 days!]

Deleted: ¶

Comment [MES9]: These are heightened efficacy claims.

Deleted: Kills 100% of Fleas in 1 hour and ticks in 3 hours¶
<#>Kills 99% of fleas and ticks after [4 weeks] [1 month]¶
<#>Kills 100% of Fleas in 1 hour and 99% after] 1 mooth] [4 weeks]¶
<#>Kills 100% of Ticks in 3 hours and 99% after[1month] [4 weeks

Deleted: <#>¶

- [Waterproof formula]
- [Dogs can be bathed 24 hours after squeeze-on is applied]

- [Reapply once every 4 weeks.] [Reapply monthly]
- [May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[NOTE: Text or images in [ ] on this label denotes optional statements and/or images that may be used on front, back, sides, top or bottom of carton/pack and/or tube label panels.]

ACTIVE INGEDIENTS:
Cyphenothrin (CAS # 39515-40-7).....40.0%
OTHER INGREDIENTS:.....60.0%
TOTAL:.....100.0%

[NOTE: Due to limited size of carton/pack labeling, the "Ingredient Statement" may be placed to "prominently" appear on the Back Carton/Pack label panel]

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [back] [or] [side] label panel[s] for additional precautionary statements

NET CONTENTS: [Three] [Six] [Twelve] 1.5 ml tubes, or
[Three] [Six] [Twelve] 3.0 ml tubes, or
[Three] [Six] [Twelve] 4.5 ml tubes, or
[Three] [Six] [Twelve] 6.0 ml tubes

Comment [MES10]: No acceptable data to support mosquitoes were provided; Dogs have neither been found to be susceptible to WNV nor suitable intermediate hosts resulting in human infection by feeding mosquitoes

Deleted: [Kills & Repels mosquitoes that are vectors of west nile virus]

Deleted: ¶

Comment [MES11]: Comparative Claims

Deleted: <#>[Longest lasting, quick acting]¶
<#>Works Stronger, Lasts Longer¶

[MASTER CARTON/PACK LABEL – BACK/SIDE PANELS]

Sergeant's Cyphenothrin
Squeeze-On for Dogs

[DO NOT USE ON CATS] [Box/icon with cat image and cross-out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling. FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or **clothing**	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.

HOTLINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS for emergency medical treatment information.

NOTE TO PHYSICIAN OR VETERINARIAN

Treat patient symptomatically

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, [snap or] cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 9 lbs. to 20 lbs.: [For cartons containing 1.5 ml applicator tubes] Apply one tube (1.5 ml) as a spot or strip to the dog's back between the shoulder blades.

For Dogs Weighing 21 lbs. to 39 lbs.: [For cartons containing two 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades.] [For cartons containing one 3.0 ml applicator tube] [Apply one tube (3.0 ml) as a spot or stripe to the dog's back between the shoulder blades.]

For Dogs Weighing 40 lbs. to 60 lbs.: [For cartons containing three 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the third tube as a spot or stripe to the dog's back directly in front of the base of the tail.] [For cartons containing one tube (4.5 ml)] [Apply one tube (4.5 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.]

For Dogs Weighing 61 lbs. and Over [For cartons containing at least four 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml) along the dog's back extending to directly in front of the base of the tail.] or [For cartons containing at lease two 3.0 ml applicator tubes] [Apply one tube (3.0 ml) as a spot or strip to the dog's back between the shoulder blades and apply the contents of the other tube (3.0 ml) along the dog's back extending to directly in front of the base of the tail.] [For cartons containing one tube (6.0 ml)] [Apply one tube (6.0 ml) as a spot or stripe to the dog's back between the shoulder blades.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Do not remove tube from the pack until ready to use. Store in a cool (below 25° C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

Pesticide Disposal: If empty: do not reuse this container. Place in trash or offer for recycling if available. If partially filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On for Dogs is an effective and easy to use product.][As with all flea and tick control products, Sergeant's Cypbenothrin Squeeze-On for Dogs should be used as part of a [an overall] [complete] program [aimed at][to][intended to][reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

Comment [MES12]: This is a heightened efficacy claim

Deleted: [Sergeant's Cyphenothrin Sqeeze-On for Dogs has demonstrated 100% control of fleas within one day of application.]

www.sergeants.com

Comment [MES13]: FYI, any language on the website is considered labeling because it is referenced on the label.

Made in the USA

[Sergeant's is committed to providing high quality products. If you have any questions or comments about this product, please write: Sergeant's Consumer Response: P.O. Box 540399, Omaha, NE 68154-0399.]

[In case of emergency, call 1-800-224-PETS.]

[WARRANTY: SERGEANT'S PET CARE, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENT MADE ON THIS LABEL.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703

[BAR CODE AREA]

EPA Reg. No. 2517-
EPA Est. No.

[MASTER LABEL-TUBE/APPLICATOR LABEL]

PANELS-

Sergeant's Cyphenothrin Squeeze-On for Dogs, [Box/Icon with cat image and cross-out], [1.5 ml] or [3.0 ml] or [4.5 ml] or [6.0 ml], Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN, EPA REG. NO. 2517-

PRODUCT PERFORMANCE / EFFICACY REVIEW
Mark Suarez, Entomologist - IB

DATE:	7 November 2006
EPA REG. NUMBER:	2517-1L 2517-IN 2517-ON
PRODUCT NAME:	Sergeant's Cyphenothrin Squeeze-On for Dogs [**2517-IL**] Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [**2517-IN**] Sergeant's Cyphenothrin + Methoprene Squeeze-On for Dogs [**2517-ON**]
REGISTRANT:	Sergeant's Pet Care Products, Inc.
PM: **REVIEWER:**	George LaRocca, PM13 Linda DeLuise
DECISION #.:	345654 [**2517-IL**] 338118 [**2517-IN**] 358246 [**2517-ON**]
DP BARCODE:	305952 [**2517-IL**] 305945 [**2517-IN**] 307614 " 319065 [**2517-ON**]
ACTION:	R26 [**2517-IL**] R31 [**2517-IN**] R26 [**2517-ON**]
ACTIVE INGREDIENT(S):	129013, Cyphenothrin.....40.0% [**2517-IL**] 129013, Cyphenothrin.....40.0% [**2517-IN**] 129032, Pyriproxyfen.....2.0% 129013, Cyphenothrin.....40.0% [**2517-ON**] 105402, s-Methoprene.....2.3%
TYPE:	Wipe-On (Squeeze-On) for Dogs
OPPTS GUIDELINE(S):	810.1000 810.3000 810.3300

MRID:	46346601 46039501 46041303 46166109 46298501 46298502 42614501 45086801 44948301 44546601 46166110
GLP ?:	No.
SITES:	Dogs; Puppies (≥12 weeks old)
PESTS:	Fleas (adult); Fleas (eggs); Fleas (larvae); Ticks; Mosquitoes; Mosquitoes (vector of WNV); Mosquitoes (vector of Heartworm); Deer Ticks (vector of Lyme Disease)
STUDY APPLICATION RATE:	variable (generally 100 mg AI/kg)
LABEL APPLICATION RATE:	Cyphenothrin [All products]: >50 mgCyphenothrin per kg dog body weight for dogs <100 lbs Pyriproxyfen [2517-IN]: >2.5 mgCyphenothrin per kg dog body weight for dogs <100 lbs s-Methoprene [2517-ON]: >2.875 mg Cyphenothrin per kg dog body weight for dogs <100 lbs

STUDY SUMMARIES:

The registrant submitted and cited a number of studies in support of three new cyphenothrin-based squeeze-on products for the protection of dogs against fleas, ticks, and mosquitoes. Each of these products contains the adulticide cyphenothrin. In addition two of the formulations [2517-IN & 2517-ON] contain an insect growth regulator (IGR). In the case of 2517-IN, the IGR is pyriproxyfen (i.e., Nylar®); in 2517-ON tbe IGR is s-Methoprene. The incorporation of an IGR is expected to enhance the effectiveness of the products by negatively affecting the development of immature stages of fleas.

Data Submited in Support of Cyphenothrin Activity

MRID 44546601. Anderson, K.; Solberg, J. 1998. Product Performance/Efficacy Reports: Evercide Pet and Plant Spray 2648: Lab Project Number: E-3459-97: 10-223-1085: 10-223-1185. Unpublished study prepared by McLaughlin Gormley King Co. 120 p.

From DER dated 27 June 2000 [No electronic copy available; tbese are the conclusions]:

"The data presented in EPA Accession (MRID) Number 44546601, having been obtained from standard laboratory and kennel testing conducted according to requirements of 95-9(a) subpart (1)-(3) on p. 263 and meeting the standards of 95-9(b)(2)(i) on p. 264 of the Product Performance Guidelines, are adequate to support the claims for killing adult fleas on contact by direct spray as summarized under Tab A in the previously mentioned volume, where a similar formulation was sprayed into a plastic pail onto *CTENOCEPHALIDES FELIS* adults on white terry cloth at 2 different area rates with 99% mortality in both cases. In a similar manner, the data summarized under Tab B in the volume are adequate to support the claims for killing ticks on contact by direct spray, where the same similar formulation is sprayed onto *RHIPICEPHALUS SANGUINEUS* on filter paper in a glass crystallizing dish with the result that 100% mortality occurred at a standard dosage of 1.0 ml. Additionally, data summarized under Tab C of the volume are adequate to support the claims for killing of fleas for 14 days and ticks for up to 7 days following trigger spray or pump spray application of a similar formulation (with lower concentration of active ingredients) to dogs of mixed sexes and weights and haircoat length as well as breeds at a rate sufficient to wet the coat to saturation, with the result that cat flea mortality was maintained at 100% for 14 days and mortality of American dog tick, *DERMACENTOR VARIABILIS*, was 100% at 3 days but fell to a marginally acceptable 81% at 7 days. Furthermore, data summarized under Tab d of the volume are adequate to support the claims for killing of fleas for 23 days and ticks for 9 days following trigger spray or pump spray application of the same similar formulation as in Tab C to cats of mixed sexes and haircoat length as well as weights at an average rate of 10.75 grams product per kilogram of pet body weight, with the result that cat flea mortality was maintained at 93% or above for 23 days and mortality of brown dog tick was maintained at or above 92% for 9 days. We will accept a claim for rapid knockdown and kill of fleas on dogs following application of the subject product at a rate sufficient to saturate the animal's coat, based on the fact that that the similar formulation resulted in 100% mortality of cat fleas at 1 hour after spraying. Finally, we will accept the claim for killing [controlling] deer ticks and other ticks [Ixodid] species

that may carry and transmit Lyme disease, on the basis of the fact that both the American dog tick and the brown dog tick are Ixodid ticks plus we have previously accepted similar formulations of permethrin and pyrethrins in combination that were effective against deer tick. -- RL Vern L. McFarland, IB"

The cited MRID could not be considered in support of the subject formulations because the test formulations were not similar to those under consideration. The test formulations contained permethrin and pyrethrins, not cyphenothrin, pyriproxyfen, or s-methoprene.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298501. Miller, T. 2003. Effect of Shampoo After Treatment with Cyphenothrin Squeeze-on on Efficacy against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Ticks (*Rhipicephalus sanguineus*) on Dogs: Analysis of Data and Conclusions. Project Number: MS/20D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 15 p.

that may carry and transmit Lyme disease, on the basis of the fact that both the American dog tick and the brown dog tick are Ixodid ticks plus we have previously accepted similar formulations of permethrin and pyrethrins in combination that were effective against deer tick. -- RL Vern L. McFarland, IB"

The cited MRID could not be considered in support of the subject formulations because the test formulations were not similar to those under consideration. The test formulations contained permethrin and pyrethrins, not cyphenothrin, pyriproxyfen, or s-methoprene.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298501. Miller, T. 2003. Effect of Shampoo After Treatment with Cypbenothrin Squeeze-on on Efficacy against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Ticks (*Rhipicephalus sanguineus*) on Dogs: Analysis of Data and Conclusions. Project Number: MS/20D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 15 p.

A squeeze-on formulation containing cyphenothrin was applied once to two groups of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*) and ticks (*Rhipicephalus sanguineus*). The dose rate was 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. The treated dogs were bathed with low detergent shampoos 12 days after treatment and wetted with water on the 19th day. No significant effect of shampoo on the residual efficacy of the spot-on was observed. Efficacy, at 90% or better compared with untreated controls, was shown against fleas for up to 16 days and against ticks for 30 days. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitoes on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate and the formulation contains 2.3% s-Methoprene, which is not in the formulation of the registration being sought. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is >11.012 mg Cyphenothrin/kg, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

MRID 46039501. Cruthers, L. 2003. Efficacy Evaluation of a Permethrin Squeeze-On Against Adult Cat Fleas (*Ctenocephalides Felis*), Adult Brown Dog Ticks (*Rhipicephalus Sanguineus*), Nymphal Deer Ticks (*Ixodes Scapularis*) and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0243. Unpublished study prepared by Professional Laboratory and Research. 79 p.

The cited study was not applicable to the registration desired. The study examined the efficacy of 45% permethrin formulations against various pet parasites.

MRID 46039501 was not considered in support of the registration of 2517-ON.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and tbe net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitos on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested witb adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is approximately > 1/10th the study dose rate, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

Data Submited in Support of Pariproxyfen Activity

MRID 42684501. Rogosheske, S. 1990. Residual Effectiveness of Nylar on Cat Flea Larvae as a Carpet/Premise Spray: Lab Project Number: F-0122-90. Unpublished study prepared by McLaughlin Gormley King Co. 16 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN because the test protocol was fundamentally different from the desired use pattern.

MRID 44948301. Schlekau, J. 1999. Product Performance/Efficacy Reports: Nylar Concentrate 2607: Lab Project Number: TL-3095: TL-3096: TL-3097. Unpublished study prepared by McLaughlin Gormley King Co. 61 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with a sbampoo or direct spray containing pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence and notable residual activity for the duration of the study (>90, for 6 to 13 months) months, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN because the test protocol was fundamentally different from the desired use pattern.

MRID 45086801. Donahue, W.; Meola, S.; Palma, K. et al. 2000. Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.

From DER dated 27 June 2000:

"CONCLUSIONS & RECOMMENDATIONS The data presented in EPA Accession (MRID) Number 450868-01, having been compiled from standard laboratory and kennel testing conducted according to requirements of § 95-9(a)(1) to (3) on p. 263 and meeting

the standard of § 95-9, subpart (b)(2)(i) on p. 264 of the Product Performance Guidelines are adequate to support claims of inhibiting the batch of larval fleas, killing of flea eggs, inhibiting the hatch of flea eggs and adversely affecting the physiological health of fleas when the subject product is diluted to produce end use products having a active ingredient [pyriproxyfen] concentration of 0.01% and 0.025% as a dip and 0.025% and 0.05% as a shampoo in the testing reported in the portion under Tab 1; are adequate to demonstrate the physiological effects of extremely low concentrations of active ingredient on the molecular structure of flea eggs exposed to pyriproxyfen in glass vials having a deposit of 0.25 mg/cm^2 as reported in the portion under Tab 2, to the extent that pyriproxyfen prevented cellular differentiation and no blastoderm had formed in eggs that were collected even more than 50 hours after exposure; are adequate to demonstrate the inhibition of egg hatch and emergence of adult fleas when eggs were exposed to either residues of 1.1 mg/cm^2 on filter paper or the same deposit on aliquots of dog hair, which were prepared by using a standard dilution of 0.007% a.i. solution, or when exposed to dog hair that had been treated with pyriproxyfen as a 0.125% spray, all of which were reported under Tab 3; and are adequate to demonstrate the following physiological effects on adults and eggs of the cat flea, *Ctenocephalides felis*, when adult fleas of both sexes were exposed to 1.1 mg AI/cm^2 on treated filter paper: histological studies of unfed fleas demonstrated that pyriproxyfen exposure caused depletion of fat body reserves and death by starvation, and fed fleas exposed to pyriproxyfen-treated dog hair also appeared to die of starvation, while eggs deposited by females in these tests were largely empty shells; additionally, studies on flea eggs suggested that pyriproxyfen was less effective as an ovicide than fenoxycarb, that pyriproxyfen exposure of newly laid eggs did not prevent hatching, but 10 minute exposure of the eggs killed 50% of fleas that developed to larval stage. These new findings, all of which were reported under Tab 4, indicated that pyriproxyfen had an unusual latent effect in which sbort-term exposure of flea eggs early in embryogenesis was often lethal to flea larvae that hatched from the egg 3 days later. In contrast, a longer-term (2-hour) exposure of eggs to pyriproxyfen produced embryocidal effects. Thus, these data are collectively adequate to demonstrate the effectiveness of pyriproxyfen formulations of various dilutions against cat flea in egg, larval and adult stages when the subject product, which is a manufacturing use concentrate, is used to prepare end use products. Specific claims are dependent upon concentration, frequency of application and various other factors whicb are beyond the scope of this review and will need to be handled on an individual case-by-case basis. It will be necessary for either the registrant or their customers wbo purchase this product for use in formulating their own end use products to provide labeling outlining the types of claims which are applicable to their formulation(s).--RL Vern L. McFarland, IB"

MRID 45086801 as per an earlier review partially supports the ovicidal and larvacidal claimsmade on the proposed label of 2517-IN. The duration of claims made (9 weeks)(63 days) could not be validated from the cited study due to differences between the test protocol and desire use pattern. The registrant may include these claims, only if it is agreed that they will submit or cite confirmatory data within 12 months.

Data Submited in Support of (S)-Methoprene Activity

MRID 46041303. Miller, T. 2003. Dose Titration of an S-Methoprene Spot-On (sic) Dogs: Final Report, Statistical Analyses and Conclusions. Unpublished study prepared in cooperation with Auburn University. 19 p.

The primary objective was to determine the dose rate of s-methoprene in a spot-on formulation that would provide one montb of residual flea ovisterilant activity on dogs: Regression-correlation analyses showed that only when the dose rate was logarithmically transformed ($\log_N$ mg/kg) was there a highly significant correlation between dose rate and duration of residual flea ovisterilant efficacy at the 90% level. The resultant regression equation predicted that a dose rate of 2.8 mg/kg provides 30 days of efficacy at 90%. The correlation between dose rate and residual efficacy at the 100% level was not statistically significant. However, flea eggs collected on day 31 from the two cats treated at the highest dose rates of 3.5 to 3.6 mg/kg were all sterile, indicating that the predicted dose rate for a 100% residual efficacy claim is near these values.

The data submitted are partially acceptable. The study dose rate (~3.5 mg/kg) and proposed dose rate (2.8 mg/kg) are consistent with the proposed label rate. The data do not fully support the desired label claim of 1 month flea ovisterilant; however, the claim is acceptable on the condition that the registrant agree to submit confirmatory data within 12 months.

ENTOMOLOGIST'S COMMENTS AND RECOMMENDATIONS:

The data submitted are marginally adequate to support the desired registrations. However, the registrant has agreed to submit or cite confirmatory data within 12 months to verify the conclusions drawn from an amalgamation of data on Cyphenothrin, Pyriproxyfen, and (S)-Methoprene. In the interim, the data are adequate to support the following claims:

EPA Reg. Nos. 2517-IL, 2517-IN, & 2517-ON

][Kills][Controls][Repels]]][Fleas][Ticks]] for up to][28 days][4 weeks][1 month]]

EPA Reg. No. 2517-IN

Kills [flea eggs][flea larvae] for up to [63 days][9 weeks].

EPA Reg. No. 2517-ON

Kills [flea eggs] for up to [24 days][4 weeks][1 month].

Additional comments are provided on the individual labels attached.

Enclosure
002557-000IN,-ON 2006NOV7
2557-IL label
2517-IN label
2517-ON label

Rick Tinsworth
<rtinsworth@exponent.com>
11/15/2006 06:15 PM

To George LaRocca/DC/USEPA/US@EPA
cc Marion Johnson/DC/USEPA/US@EPA, Lois Rossi/DC/USEPA/US@EPA, Mark Suarez/DC/USEPA/US@EPA
bcc
Subject FW: Revised Sergeant's Labels

george

as requested we are submitting revised labels per the epa reviews - there are 2 exceptions to the requested language which i would ask you to consider

1. the reviews indicated we could say "begins (or starts) to kill and repel fleas in as little as one hour" and "begins (or starts) to kill and repel ticks in as little as 3 hours"

we would much prefer to say "kills (and repels) fleas in as little as 1 hour" and "kills (and repels) ticks in as little as 3 hours"

from our perspective the preferred language would help from a marketing perspective and conveys the same message suggested by epa

2. we were told to remove language related to west nile virus and mosquitoes - we have deleted the west nile virus language

however we urgently request your approval - to drop language that states "kills mosquitoes for up to 30 days" and to replace it with "kills (and repels) mosquitoes"

you are allowing a 4 week claim on fleas and ticks subject to conducting a new study as a condition of registration

the epa review says there are no acceptable data for mosquitoes - we agree mosquitoes were not covered in the dose titration study but there is in fact a study that demonstrates good efficacy at 100 mg/kg re mortality and preventing feeding - we understand it would have been mcu preferred to have mosquitoes included in the dose titration study - but ask that you consider our critical need to be able to have some statement re mosquitoes

we do not propose to indicate any time period - merely to say the products "kills (and repels) mosquitoes"

WITHOUT A MOSQUITOES CLAIM - WE DO NOT HAVE A SELLABLE PRODUCT

we request that you allowed the claim with no time period and we will certainly agree to include mosquitoes in the new study that will be conducted as a condition of registration

please let us know as soon as possible concerning both these requests - again if we are to have a product on wallmart shelves next season we must have a registration very soon and we must have the claims requested

we are ready to discuss these issues with you at your convenience.

thank you for your assistance in this matter

Rick Tinsworth
202-772-4912
NOTE NEW CELL PHONE NUMBER - 202-6t5-7436

From: James Messina
Sent: Wednesday, November 15, 2006 12:21 PM
To: Rick Tinsworth
Subject: Revised Sergeant's Labels

James Messina
Senior Managing Regulatory Consultant
Exponent
Food and Chemicals Practice
1730 Rhode Island Avenue, N.W.
Suite t100
Washington, DC 20036
202-772-4932
202-772-4979 fax

2517-ON Cyphenothrin + methoprene 111506 Final Label.doc

2517-IL Cyphenothrin + Nylar 111506 final label.doc

2517-IL Cyphenothrin Only Label 111506 final.doc

Rick Tinsworth
<rtinsworth@exponent.com>
11/15/2006 06:19 PM

To George LaRocca/DC/USEPA/US@EPA, Mark Suarez/DC/USEPA/US@EPA
cc James Messina <jmessina@exponent.com>
bcc
Subject efficacy reviews for cyphenothrin

george and mark

pls note the following

we do not see any review for the dose titration study

we see reviews for a number of studies that mark indicates are not relevant for the pending registrations - we don't disagree - we just can't figure out why the studies were reviewed - to the best of our knowledge these studies were not listed in the data matrices submitted with the applications - we would appreciate any clarification

last, mark consistently indicates that the label dose rate is > 5.14 mg/kg - we assume that the decimal is misplaced and that mark now agrees that the statement should be > 51.4 mg/kg

thanks

Rick Tinsworth
202-772-4912
NOTE NEW CELL PHONE NUMBER - 202-615-7436

THANKS GEORGE - ME REVIEW AND I WILL GET BACK TO YOU

-----Original Message-----
From: LaRocca.George@epamail.epa.gov
[mailto:LaRocca.George@epamail.epa.gov]
Sent: Monday, November 13, 2006 3:19 PM
To: Rick Tinsworth
Cc: johnson.marion@epamail.epa.gov
Subject: Re: CAN I GET AN UDATE ON THE SERGEANTS REGISTRATION

Rick,

I am attaching a copy of Mark Suarez review of the efficacy data submmitted/cited and comments on the latest labels. Due to the large number of comments regarding the marketing claims I am asking you to resubmit a corrected clean copy of the labeling. The data submitted are marginally adequate to support the desired registrations. However, Sergeants has agreed to submit or cite confirmatory data within 12 months to verify the conclusions drawn from an amalgamation of data on Cyphenothrin, Pyriproxyfen, and (S)-Methoprene. In the interim, the data are adequate to support the following claims:

EPA Reg. Nos. 2517-IL, 2517-IN, & 2517-ON
[[Kills][Controls][Repels]] [[Fleas][Ticks]] for up to [[28 days][4 weeks][1 month]]
lea eggs][flea larvae] for up to [63 days][9 weeks].

EPA Reg. No. 2517-ON
Kills [flea eggs] for up to [24 days][4 weeks][1 month].

See the individual labels for specific comments beginning on pg 11 of the EPA review. Thanks.

(See attached file: 002517-000IN.-ON 2006NOV7.doc]

George LaRocca, PM 13
Insecticides Branch
Registration Division
Office of Pesticides Programs, US EPA
703-305-6100
larocca.george@epa.gov
Visit: http://www.epa.gov/pesticides/

Rick Tinsworth
<rtinsworth@exponent.com>

11/13/2006 12:44 PM

To: George LaRocca/DC/USEPA/US@EPA, Marion Johnson/DC/USEPA/US@EPA
cc:
Subject: CAN I GET AN UDATE ON THE SERGEANTS REGISTRATION

george and marion -

in our last conf call you hoped that a registration could be completed last week

can you pls let me know when the registration will be done - timing is critical - we need to show walmart we actually have the registrations

thanks

Rick Tinsworth
202-772-4912
NOTE NEW CELL PHONE NUMBER - 202-615-7436

Rick Tinsworth
<rtinsworth@exponent.com>
11/13/2006 03:22 PM

To George LaRocca/DC/USEPA/US@EPA
cc
bcc
Subject RE: CAN I GET AN UDATE ON THE SERGEANTS REGISTRATION

James Messina <jmessina@exponent.com>
10/31/2006 12:59 PM

To: Mark Suarez/DC/USEPA/US@EPA, George LaRocca/DC/USEPA/US@EPA, Marion Johnson/DC/USEPA/US@EPA
cc: lnouvel@covad.net, BScharf@SERGEANTS.COM, Rick Tinsworth <rtinsworth@exponent.com>
bcc:
Subject: Cyphenothrin

Mark and George,

I have spoken with Sergeant's and have the following clarifications that I would like to discuss with you on the phone:

1. Attached is a summary of the dose titration study. Low dose 25 mg/kg, high dose 96 mg/kg. We believe the data support an "upto" efficacy claim on fleas and ticks of 45 days. Historically the Agency has accepted similar data to support an "upto" efficacy claim.

2. Attached is also a summary of the application rates for the draft label on file with EPA and the proposed revised label. The current draft label does not have an application rate that is lower than 33 mg/kg. It also does not have any dose that exceeds the single dose rate from the DASS. The proposed revised application rates do not have an application rate lower than 51 mg/kg. Also the proposed label does not have any dose that exceeds the single dose rate from the DASS.

3. The proposed label also only offers application to >9 lbs. dogs.

We believe that the dose titration study supports the current and proposed label with upto claims for 45 days. The Agency has accepted similar data to support upto label claims for other products as well.

Can we please discuss this information in more detail on the phone today. I will try to reach you shortly.

We appreciate the effort the Agency is making towards registration and hope that we can resolve things today.

Best Regards,

James Messina
Senior Managing Regulatory Consultant
Exponent
Food and Chemicals Practice
1730 Rhode Island Avenue, N.W.
Suite 1100

≥9 lb ?

45% 5 weeks

less than 120% amounts

90%

etophenprox

Washington, DC 20036
202-772-4932
202-772-4979 fax


cyphenspotdogdosechart4 rev 093006.xls


summary efficacies.xls

Exponent

Exponent
1730 Rhode Island Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

October 25, 2006

George T. LaRocca
Product Manager (13)
Insecticide Branch, Registration Division
United States Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, Virginia 22202

Subject: Cyphenothrin Pending EPA Registrations and
Review of Sergeant's Pet Products, Inc. Draft Protocol
Project No. WD00758.000

Dear Mr. LaRocca:

On behalf of our client, Sergeant's Pet Products, Inc. (Sergeant's), Exponent is confirming for EPA that Sergeant's plans to conduct a cyphenothrin-specific dislodgeability study according to EPA's revised protocol. Additionally, Sergeant's is submitting the enclosed response to the Agency's comments and additions to Sergeant's Draft Protocol, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation," which were detailed in a memorandum from EPA dated September 21, 2006.

Sergeant's agrees to conduct a cyphenothrin-specific dislodgeability study according to EPA's revised protocol. Sergeant's will initiate the study once it receives final feedback from EPA on the questions/clarifications for the study protocol listed in this letter and will submit a final report to EPA within nine (9) months of initiation.

Sergeant's has several questions/clarifications related to the Agency's comments on the study protocol. Several of the revisions to the protocol appear to be inconsistent with previous EPA policy for similar studies. Sergeant's respectfully requests further explanation for the differences from previous protocol requirements as outlined below.

- EPA has amended the protocol to require application via syringe, rather than from the final package in which the product will be distributed, as was previously required. To maximize flexibility for the registrant, Sergeant's requests that the Agency allow application via either final packaging or a syringe as appropriate.

- The addition of the pilot/preliminary 5 dog study and the "hand to mouth" component to the experimental study significantly increase the number of animals required, but the scientific benefit of these components, if any, may not be worth the extra cost. Typical EPA pet animal protocols require a minimum of 6 subjects per test group. However, with the "pet hug" and "hand to mouth" scenarios, a total of 20 dogs will be used. Furthermore, the additional cost of the 25 required laboratory-bred Beagles is prohibitive for a study of this nature.

- The protocol for the pilot/preliminary 5 dog study does not provide sufficient detail to ensure that the determinations of the Study Director regarding the procedures for the field portion of the study will be acceptable to the Agency upon review. The decision appears to be subjective; therefore, we request that the Agency provide clearer guidance. Specifically, EPA should articulate the criterion by which the appropriate number of stroking simulations to be performed will be determined.

- In the hand to mouth portion of the experimental study added by the Agency, the protocol indicates that sampling may be discontinued if and when two non-detect samples are identified from the results of all glove samples for a given time period analysis. However, for this portion of the study there is only one petting simulation that takes place at 24 hours after the application of the product to the dogs. Therefore, the discontinuance statements should be omitted from the protocol for the hand to mouth component.

- EPA states that the second cotton glove will be used to determine if breakthrough is occurring and that analysis of the nitrile glove will be required only when breakthrough is observed. EPA should clarify how the analytical results from the various gloves will be "combined" (as indicated in A.9). Will ½ the LOQ or LOD be added for all non-quantifiable or non-detectable residues from all three glove layers? This could be exceedingly conservative in some cases. EPA should clarify how glove analyses will be combined and analyzed,

- Finally, Sergeant's wishes to raise the issue of terminology. In the protocol provided, the words "simulation" and "replicates" are used interchangeably and also in distinct fashions. Sergeant's suggests that the word "replicate" be associated with the number of dogs (i.e., data gathered from 10 dogs will constitute 10 replicates) and that the term "stroking procedure" be introduced, such that a "simulation" will consist of X stroking procedures (where X is determined in the pilot study and the stroking procedure is defined as in the current protocol). Sergeant's believes that these or similar changes in the terminology will improve the protocol.

- Based on discussions with Agency personnel, Sergeant's understanding is that the use of the latex glove under the cotton glove removes the dislodgeability study from consideration of the human testing review board. Please provide confirmation if this is the Agency's understanding as well.

- In addition to the above comments specific the use of this protocol to support Sergeant's pending registration, Sergeant's would like to add a general comment regarding this protocol as it may be used for other registrants or future Sergeant's products. While it seems intuitive that the transferable fractions measured for the "pet hug" and "hand to mouth" scenarios will be different (due to the likely less intensive contact associated with the hand to mouth scenario), one avenue to reduce the costs of this study would be to allow registrants to conduct only the hug scenario. Sergeant's suggests that the protocol include the flexibility for registrants to decide whether to generate specific data for just the hug scenario or for both the hug and hand to mouth scenario.

We look forward to discussing our questions and comments with the Agency to finalize this protocol. I may be reached via telephone at (202) 772-4932 or via email at jmessina@exponent.com.

Sincerely,

James Messina
Managing Regulatory Consultant

cc: Larry Nouvel

James Messina
<jmessina@exponent.com>
10/25/2006 03:52 PM

To George LaRocca/DC/USEPA/US@EPA
cc Rick Tinsworth <rtinsworth@exponent.com>, lnouvel@covad.net, Carrie Daniels <cdaniels@exponent.com>, Jason Johnston
bcc
Subject Cyphenothrin

Mr. LaRocca,

Please find attached a letter to EPA. The letter confirms Sergeant's intent to conduct a cyphenothrin specific dislodgeability study according to the new protocol. It also includes some comments and questions on the new study protocol that require EPA's attention. We look forward to the Agency's response.

Best Regards,

James Messina
Senior Managing Regulatory Consultant
Exponent
Food and Chemicals Practice
1730 Rhode Island Avenue, N.W.
Suite t100
Washington, DC 20036
202-772-4932
202-772-4979 fax

Sergeant's Letter to EPA Cyphenothrin.pdf

Submi[illegible] label, grouping unit dose delive[illegible]

Squeeze-On Dose Volume/Dose Rate Chart: Deliverable Product

Potency w/w Cyphenothrin 40.00%
Nylar 2.00%

Weight		Dose			Weight		Dose		
lb	kg	mL	mg/kg		lb	kg	mL	mg/kg	
			Cyphenothrin	Nylar				Cyphenothrin	Nylar
1	0.5	0.7	617	30.9	50	22.7	2.7	48	2.4
2	0.9	0.7	309	15.4	51	23.1	2.7	47	2.3
3	1.4	0.7	206	10.3	52	23.6	2.7	46	2.3
4	1.8	0.7	154	7.7	53	24.0	2.7	45	2.2
5	2.3	0.7	123	6.2	54	24.5	2.7	44	2.2
6	2.7	0.7	103	5.1	55	24.9	2.7	43	2.2
7	3.2	0.7	88	4.4	56	25.4	2.7	43	2.1
8	3.6	0.7	77	3.9	57	25.9	2.7	42	2.1
9	4.1	0.7	69	3.4	58	26.3	2.7	41	2.1
10	4.5	0.7	62	3.1	59	26.8	2.7	40	2.0
11	5.0	0.7	56	2.8	60	27.2	2.7	40	2.0
12	5.4	0.7	51	2.6	61	27.7	2.7	39	2.0
13	5.9	0.7	47	2.4	62	28.1	2.7	38	1.9
14	6.4	0.7	44	2.2	63	28.6	2.7	38	1.9
15	6.8	1.2	71	3.5	64	29.0	2.7	37	1.9
16	7.3	1.2	66	3.3	65	29.5	2.7	37	1.8
17	7.7	1.2	62	3.1	66	29.9	4.2	56	2.8
18	8.2	1.2	59	2.9	67	30.4	4.2	55	2.8
19	8.6	1.2	56	2.8	68	30.8	4.2	54	2.7
20	9.1	1.2	53	2.6	69	31.3	4.2	54	2.7
21	9.5	1.2	50	2.5	70	31.8	4.2	53	2.6
22	10.0	1.2	48	2.4	71	32.2	4.2	52	2.6
23	10.4	1.2	46	2.3	72	32.7	4.2	51	2.6
24	10.9	1.2	44	2.2	73	33.1	4.2	51	2.5
25	11.3	1.2	42	2.1	74	33.6	4.2	50	2.5
26	11.8	1.2	41	2.0	75	34.0	4.2	49	2.5
27	12.2	1.2	39	2.0	76	34.5	4.2	49	2.4
28	12.7	1.2	38	1.9	77	34.9	4.2	48	2.4
29	13.2	1.2	36	1.8	78	35.4	4.2	47	2.4
30	13.6	1.2	35	1.8	79	35.8	4.2	47	2.3
31	14.1	1.2	34	1.7	80	36.3	4.2	46	2.3
32	14.5	1.2	33	1.7	81	36.7	4.2	46	2.3
33	15.0	2.7	72	3.6	82	37.2	4.2	45	2.3
34	15.4	2.7	70	3.5	83	37.6	4.2	45	2.2
35	15.9	2.7	68	3.4	84	38.1	4.2	44	2.2
36	16.3	2.7	66	3.3	85	38.6	4.2	44	2.2
37	16.8	2.7	64	3.2	86	39.0	4.2	43	2.2
38	17.2	2.7	63	3.1	87	39.5	4.2	43	2.1
39	17.7	2.7	61	3.1	88	39.9	4.2	42	2.1
40	18.1	2.7	60	3.0	89	40.4	4.2	42	2.1
41	18.6	2.7	58	2.9	90	40.8	4.2	41	2.1
42	19.1	2.7	57	2.8	91	41.3	4.2	41	2.0
43	19.5	2.7	55	2.8	92	41.7	4.2	40	2.0
44	20.0	2.7	54	2.7	93	42.2	4.2	40	2.0
45	20.4	2.7	53	2.6	94	42.6	4.2	39	2.0
46	20.9	2.7	52	2.6	95	43.1	4.2	39	1.9
47	21.3	2.7	51	2.5	96	43.5	4.2	39	1.9
48	21.8	2.7	50	2.5	97	44.0	4.2	38	1.9
49	22.2	2.7	49	2.4	98	44.5	4.2	38	1.9

Max DASS dose rates, mg/kg

Propose a[illegible]nded label, grouping unit dose d[illegible]very

Squeeze-On Dose Volume/Dose Rate Chart: Deliverable Product

Potency w/w Cyphenothrin 40.00% **maintains 4 SKU's & range rates >50 & < DASS single rate**

Nylar 2.00%

Weight		Dose			Weight		Dose		
lb	kg	mL	mg/kg		lb	kg	mL	mg/kg	
			Cyphenothrin	Nylar				Cyphenothrin	Nylar
					50	22.7	4.2	74	[illegible]
					51	23.1	4.2	73	[illegible]
					52	23.6	4.2	71	[illegible]
					53	24.0	4.2	70	[illegible]
					54	24.5	4.2	69	[illegible]
					55	24.9	4.2	67	[illegible]
					56	25.4	4.2	66	[illegible]
					57	25.9	4.2	65	[illegible]
9	4.1	1.2	118	[illegible]	58	26.3	4.2	64	[illegible]
10	4.5	1.2	106		59	26.8	4.2	63	[illegible]
11	5.0	1.2	96	[illegible]	60	27.2	4.2	62	[illegible]
12	5.4	1.2	88	[illegible]	61	27.7	5.7	82	[illegible]
13	5.9	1.2	81	[illegible]	62	28.1	5.7	81	[illegible]
14	6.4	1.2	76	[illegible]	63	28.6	5.7	80	[illegible]
15	6.8	1.2	71	[illegible]	64	29.0	5.7	79	[illegible]
16	7.3	1.2	66	[illegible]	65	29.5	5.7	77	[illegible]
17	7.7	1.2	62	[illegible]	66	29.9	5.7	76	[illegible]
18	8.2	1.2	59	[illegible]	67	30.4	5.7	75	[illegible]
19	8.6	1.2	56	[illegible]	68	30.8	5.7	74	[illegible]
20	9.1	1.2	53	[illegible]	69	31.3	5.7	73	[illegible]
21	9.5	2.7	113	[illegible]	70	31.8	5.7	72	[illegible]
22	10.0	2.7	108	[illegible]	71	32.2	5.7	71	[illegible]
23	10.4	2.7	104	[illegible]	72	32.7	5.7	70	[illegible]
24	10.9	2.7	99	[illegible]	73	33.1	5.7	69	[illegible]
25	11.3	2.7	95		74	33.6	5.7	68	[illegible]
26	11.8	2.7	92	[illegible]	75	34.0	5.7	67	[illegible]
27	12.2	2.7	88	[illegible]	76	34.5	5.7	66	[illegible]
28	12.7	2.7	85	[illegible]	77	34.9	5.7	65	[illegible]
29	13.2	2.7	82		78	35.4	5.7	64	[illegible]
30	13.6	2.7	79		79	35.8	5.7	64	[illegible]
31	14.1	2.7	77	[illegible]	80	36.3	5.7	63	[illegible]
32	14.5	2.7	74	[illegible]	81	36.7	5.7	62	[illegible]
33	15.0	2.7	72	[illegible]	82	37.2	5.7	61	[illegible]
34	15.4	2.7	70	[illegible]	83	37.6	5.7	61	[illegible]
35	15.9	2.7	68	[illegible]	84	38.1	5.7	60	[illegible]
36	16.3	2.7	66		85	38.6	5.7	59	[illegible]
37	16.8	2.7	64	[illegible]	86	39.0	5.7	58	[illegible]
38	17.2	2.7	63	[illegible]	87	39.5	5.7	58	[illegible]
39	17.7	2.7	61	[illegible]	88	39.9	5.7	57	[illegible]
40	18.1	4.2	93	[illegible]	89	40.4	5.7	56	[illegible]
41	18.6	4.2	90	[illegible]	90	40.8	5.7	56	[illegible]
42	19.1	4.2	88		91	41.3	5.7	55	
43	19.5	4.2	86	[illegible]	92	41.7	5.7	55	[illegible]
44	20.0	4.2	84	[illegible]	93	42.2	5.7	54	[illegible]
45	20.4	4.2	82		94	42.6	5.7	53	
46	20.9	4.2	81	[illegible]	95	43.1	5.7	53	[illegible]
47	21.3	4.2	79	[illegible]	96	43.5	5.7	52	[illegible]
48	21.8	4.2	77	[illegible]	97	44.0	5.7	52	[illegible]
49	22.2	4.2	76	3.8	98	44.5	5.7	51	[illegible]

g		Cyphenothrin	Nylar		Cyphenothrin	Nylar
	1X	123	9		123	9
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Decision #: 338118

DATA PACKAGE BEAN SHEET

DP #: (334181)

Date: 16-Nov-2006

* * * Registration Information * * *

Registration: 2517-IN - SERGEANT'S CYPHENOTHRIN + IGR SQUEEZE-ON FOR DOG

Company: 2517 - SERGEANT'S PET CARE PRODUCTS, INC.

Risk Manager: RM 13 - George Larocca - (703) 305-6100 Room# PY1 S-7219

Risk Manager Reviewer: George Larocca GLAROCCA

Sent Date: _____ Calculated Due Date: 13-Feb-2007 Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (R26,4) NEW USE;NON-FOOD;INDOOR;

Ingredients: 129032, Pyriproxyfen(2%)

129013, Cyphenothrin(40%)

* * * Data Package Information * * *

Expedite: ● Yes ○ No Date Sent: 16-Nov-2006 Due Back: _____

DP Ingredient: t29013, Cyphenothrin

129032, Pyriproxyfen

DP Title: _____

CSF Included: ○ Yes ● No Label Included: ● Yes ○ No Parent DP #: _____

	Assigned To	Date In	Date Out	
Organization:	RD / TRB			Last Possible Science Due Date: 15-Dec-2006
Team Name:	TOX			Science Due Date:
Reviewer Name:	Backus, Byron			Sub Data Package Due Date:
Contractor Name:				

* * * Studies Sent for Review * * *

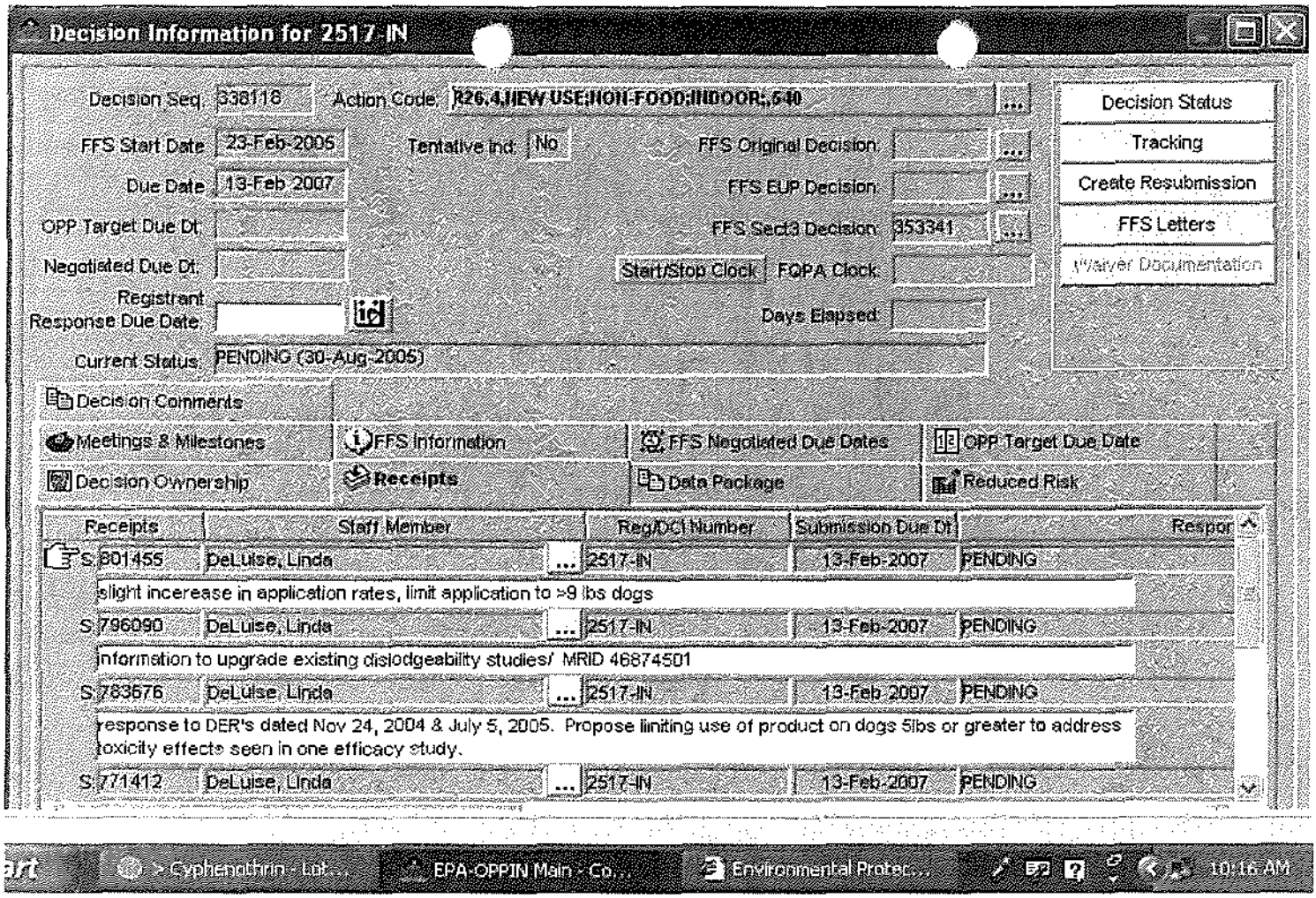
No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 2

* * * Data Package Instructions * * *

Attention Byron Backus - Due to lack of efficacy at lower application rate applicant has increased application rate and limited use to >9 lb dogs. Applicant claims that this increase does not affect the results of our review of the DASS. See attached e-mail. I previously provided you with copies of your reviews and summary of the applicants previous and proposed application rates. Would appreciate it if you can provide your comment(s) by next week orally if posible. Thanks. ifyou need any additional info please contact me. G. LaRocca.


Decision Information for 2517-IN
Decision Seq: 338118
Action Code: R26,4,NEW USE;NON-FOOD;INDOOR;,540
FFS Start Date: 23-Feb-2006
Tentative Ind: No
FFS Original Decision:
Due Date: 13-Feb-2007
FFS EUP Decision:
OPP Target Due Dt:
FFS Sect3 Decision: 353341
Negotiated Due Dt:
Start/Stop Clock
FQPA Clock:
Registrant Response Due Date:
Days Elapsed:
Current Status: PENDING (30-Aug-2005)
Decision Status
Tracking
Create Resubmission
FFS Letters
Waiver Documentation
Decision Comments
Meetings & Milestones
FFS Information
FFS Negotiated Due Dates
OPP Target Due Date
Decision Ownership
Receipts
Data Package
Reduced Risk
Receipts
Staff Member
Reg/DCI Number
Submission Due Dt
Respor
S 801455
DeLuise, Linda
2517-IN
13-Feb-2007
PENDING
slight incerease in application rates, limit application to >9 lbs dogs
S 796090
DeLuise, Linda
2517-IN
13-Feb-2007
PENDING
information to upgrade existing dislodgeability studies/ MRID 46874501
S 783676
DeLuise, Linda
2517-IN
13-Feb-2007
PENDING
response to DER's dated Nov 24, 2004 & July 5, 2005. Propose limiting use of product on dogs 5lbs or greater to address toxicity effects seen in one efficacy study.
S 771412
DeLuise, Linda
2517-IN
13-Feb-2007
PENDING
> Cyphenothrin - Lot...
EPA-OPPIN Main - Co...
Environmental Protec...
10:16 AM

Rick Tinsworth
<rtinsworth@exponent.com>
11/02/2006 11:24 AM

To George LaRocca/DC/USEPA/US@EPA, Mark Suarez/DC/USEPA/US@EPA, Marion Johnson/DC/USEPA/US@EPA
cc bscharf@sergeants.com
bcc
Subject sergeants

george et al

attached are the following pdf npirs runs showing studies and mrid numbers re efficacy of etofenprox - relevant studies are shown by check mark - the sergeants registrations are 69332-3-2517 and 69332-4-2517 - in addition a copy of one of the studies is attached - these are recent registrations with recent data -

in addition - sergeants has the following permethrin registrations 2517-87 and 69332-1-2517 supported by studies with mrid numbers 46039501 and 46281101 - a pdf of one of the studies is also attached

sergeants also refers epa to a cutter permethrin registration 73510-8-1903 supported by efficacy studies with mrid numbers of 25364808 and 26425801 - up to 5 weeks claim is a recent amendment

these registrations and supporting data are relevant to the discussion we had yesterday re the up to claims - **in our view the up to claims are not based on mean values**

also attached are 2 data sheets related to the 3 data points we have for the cyphenothrin data - 25 - 85 and 100 mg - mark has seen 2 data points - 25 and 100 - we have a third at 85 - and have done analysis using the 3 data points

we are prepared to discuss each of the attachments re the up to claims this afternoon in a conf call

we are also prepared to explain the data sheets that dr tom miller prepared and that are attached - to support a possible compromise position as follows

we believe the data support the up to claims we requested and we believe the attached data support the level playing field argument we made yesterday

nevertheless we offer the following compromise proposal

an up to claim of 5 weeks for fleas and 6 weeks for ticks based on our existing data and including the analysis by dr miller which is attached

we will conduct additional efficacy work at 50 mg as a condition of registration conditional registration

we would prefer to stay at the original proposed appl rates but will increase them as shown in the table provided to george and mark yesterday increase as shown

PRODUCT PERFORMANCE / EFFICACY REVIEW
Mark Suarez, Entomologist - 1B

DATE:	26 September 2006
EPA REG. NUMBER:	2517-IN 2517-ON
PRODUCT NAME:	Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [**2517-IN**] Sergeant's Cyphenothrin + Methoprene Squeeze-On for Dogs [**2517-ON**]
REGISTRANT:	Sergeant's Pet Care Products, Inc.
PM: **REVIEWER:**	George LaRocca, PM13 Linda DeLuise
DECISION #.:	338118 [**2517-IN**] 358246 [**2517-ON**]
DP BARCODE:	305945 [**2517-IN**] 307614 " 319065 [**2517-ON**]
ACTION:	R31 [**2517-IN**] R26 [**2517-ON**]
ACTIVE INGREDIENT(S):	129013, Cyphenothrin.....40.0% [**2517-IN**] 129032, Pyriproxyfen.....2.0% 129013, Cyphenothrin.....40.0% [**2517-ON**] 105402, s-Methoprene.....2.3%
TYPE:	Wipe-On (Squeeze-On) for Dogs
OPPTS GUIDELINE(S):	810.1000 810.3000 810.3300
MRID:	46346601 46039501 46041303 46166109 46298501 46298502 42614501 45086801

MRIDs [cont.]	44948301 44546601
GLP ?:	No.
SITES:	Dogs; Puppies (≥12 weeks old)
PESTS:	Fleas (adult); Fleas (eggs); Fleas (larvae); Ticks; Mosquitoes; Mosquitoes (vector of WNV); Mosquitoes (vector of Heartworm); Deer Ticks (vector of Lyme Disease)
STUDY APPLICATION RATE:	variable (generally 100 mg AI/kg)
LABEL APPLICATION RATE:	Cyphenothrin: <15 kg: 1.0mL (>3.43 mg AI/kg)* 15-33kg: 1.5mL (2.38 – 5.14 mg AI/kg) 33-66kg: 3.0mL (2.34 – 4.68 mg AI/kg) >66kg: 4.5mL (<3.51 mg AI/kg) Pyriproxyfen: <15 kg: 1.0mL (>0.171 mg AI/kg)* 15-33kg: 1.5mL (0.117 – 0.257 mg AI/kg) 33-66kg: 3.0mL (0.117 – 0.234 mg AI/kg) >66kg: 4.5mL (<0.175 mg AI/kg) s-Methoprene: <15 kg: 1.0mL (>0.197 mg AI/kg)* 15-33kg: 1.5mL (0.134 – 0.296 mg AI/kg) 33-66kg: 3.0mL (0.134 – 0.269 mg AI/kg) >66kg: 4.5mL (<0.202 mg AI/kg)

* 40% Cypermethrin w/w, 2.0% Pyriproxyfen w/w, 2.3% s-Methoprene w/w; Specific Gravity of the formulation = 1.073 lb/gal

STUDY SUMMARIES:

The registrant submitted and cited a number of studies in support of two new cyphenothrin-based squeeze-on products for the protection of dogs against fleas, ticks, and mosquitoes. Each of these products contains the adulticide cyphenothrin, in addition to an insect growth regulator (IGR). In the case of 2517-IN, the IGR is pyriproxyfen (i.e., Nylar®); in 2517-ON the IGR is s-Methoprene. The incorporation of an IGR is expected to enhance the effectiveness of the product by negatively affecting the development of immature stages of fleas.

Data Support for 2517-IN

MRID 42684501. Rogosheske, S. 1990. Residual Effectiveness of Nylar on Cat Flea Larvae as a Carpet/Premise Spray: Lab Project Number: F-0122-90. Unpublished study prepared by McLaughlin Gormley King Co. 16 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN.

MRID 44546601. Anderson, K.; Solberg, J. 1998. Product Performance/Efficacy Reports: Evercide Pet and Plant Spray 2648: Lab Project Number: E-3459-97: 10-223-1085: 10-223-1185. Unpublished study prepared by McLaughlin Gormley King Co. 120 p.

From DER dated 27 June 2000 [No electronic copy available; these are the conclusions]:

"The data presented in EPA Accession (MRID) Number 44546601, having been obtained from standard laboratory and kennel testing conducted according to requirements of 95-9(a) subpart (1)-(3) on p. 263 and meeting the standards of 95-9(b)(2)(i) on p. 264 of the Product Performance Guidelines, are adequate to support the claims for killing adult fleas on contact by direct spray as summarized under Tab A in the previously mentioned volume, where a similar formulation was sprayed into a plastic pail onto *CTENOCEPHALIDES FELIS* adults on white terry cloth at 2 different area rates with 99% mortality in both cases. In a similar manner, the data summarized under Tab B in the volume are adequate to support the claims for killing ticks on contact by direct spray, where the same similar formulation is sprayed onto *RHIPICEPHALUS SANGUINEUS* on filter paper in a glass crystallizing dish with the result that 100% mortality occurred at a standard dosage of 1.0 ml. Additionally, data summarized under Tab C of the volume are adequate to support the claims for killing of fleas for 14 days and ticks for up to 7 days following trigger spray or pump spray application of a similar formulation (with lower concentration of active ingredients) to dogs of mixed sexes and weights and haircoat length as well as breeds at a rate sufficient to wet the coat to saturation, with the result that cat flea mortality was maintained at 100% for 14 days and mortality of American dog tick, *DERMACENTOR VARIABILIS*, was 100% at 3 days but fell to a marginally acceptable 81% at 7 days. Furthermore, data summarized under Tab d of the volume are adequate to support the claims for killing of fleas for 23 days and ticks for 9 days following trigger spray or pump spray application of the same similar formulation as in Tab C to cats of mixed sexes and haircoat length as well as weights at an average rate of 10.75 grams product per kilogram of pet body weight, with the result that cat flea mortality was maintained at 93% or above for 23 days and mortality of brown dog tick was maintained at or above 92% for 9 days. We will accept a claim for rapid knockdown and kill of fleas on dogs following application of the subject product at a rate sufficient to saturate the animal's coat, based on the fact that that the similar

formulation resulted in 100% mortality of cat fleas at 1 hour after spraying. Finally, we will accept the claim for killing [controlling] deer ticks and other ticks [Ixodid] species that may carry and transmit Lyme disease, on the basis of the fact that both the American dog tick and the brown dog tick are Ixodid ticks plus we have previously accepted similar formulations of permethrin and pyrethrins in combination that were effective against deer tick. -- RL Vern L. McFarland, IB"

The cited MRID could not be considered in support of the subject formulations because the test formulations were not similar to those under consideration. The test formulations contained permethrin and pyrethrins, not cyphenothrin, pyriproxyfen, or s-methoprene.

MRID 44948301. Schlekau, J. 1999. Product Performance/Efficacy Reports: Nylar Concentrate 2607: Lab Project Number: TL-3095: TL-3096: TL-3097. Unpublished study prepared by McLaughlin Gormley King Co. 61 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with a shampoo or direct spray containing pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence and notable residual activity for the duration of the study (>90, for 6 to 13 months) months, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN.

MRID 45086801. Donahue, W.; Meola, S.; Palma, K. et al. 2000. Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.

From DER dated 27 June 2000:

"CONCLUSIONS & RECOMMENDATIONS The data presented in EPA Accession (MRID) Number 450868-01, having been compiled from standard laboratory and kennel testing conducted according to requirements of § 95-9(a)(1) to (3) on p. 263 and meeting the standard of § 95-9, subpart (b)(2)(i) on p. 264 of the Product Performance Guidelines are adequate to support claims of inhibiting the hatch of larval fleas, killing of flea eggs, inhibiting the hatch of flea eggs and adversely affecting the physiological health of fleas when the subject product is diluted to produce end use products having a active ingredient [pyriproxyfen] concentration of 0.01% and 0.025% as a dip and 0.025% and 0.05% as a shampoo in the testing reported in the portion under Tab 1; are adequate to demonstrate the physiological effects of extremely low concentrations of active ingredient on the molecular structure of flea eggs exposed to pyriproxyfen in glass vials having a deposit of 0.25 mg/cm^2 as reported in the portion under Tab 2, to the extent that pyriproxyfen prevented cellular differentiation and no blastoderm had formed in eggs that were collected even more than 50 hours after exposure; are adequate to demonstrate the inhibition of egg hatch and emergence of adult fleas when eggs were exposed to either

residues of 1.1 mg/cm^2 on filter paper or the same deposit on aliquots of dog hair, which were prepared by using a standard dilution of 0.007% a.i. solution, or when exposed to dog hair that had been treated with pyriproxyfen as a 0.125% spray, all of which were reported under Tab 3; and are adequate to demonstrate the following physiological effects on adults and eggs of the cat flea, *Ctenocephalides felis*, when adult fleas of both sexes were exposed to 1.1 mg AI/cm^2 on treated filter paper: histological studies of unfed fleas demonstrated that pyriproxyfen exposure caused depletion of fat body reserves and death by starvation, and fed fleas exposed to pyriproxyfen-treated dog hair also appeared to die of starvation, while eggs deposited by females in these tests were largely empty shells; additionally, studies on flea eggs suggested that pyriproxyfen was less effective as an ovicide than fenoxycarb, that pyriproxyfen exposure of newly laid eggs did not prevent hatching, but 10 minute exposure of the eggs killed 50% of fleas that developed to larval stage. These new findings, all of which were reported under Tab 4, indicated that pyriproxyfen had an unusual latent effect in which short-term exposure of flea eggs early in embryogenesis was often lethal to flea larvae that hatched from the egg 3 days later. In contrast, a longer-term (2-hour) exposure of eggs to pyriproxyfen produced embryocidal effects. Thus, these data are collectively adequate to demonstrate the effectiveness of pyriproxyfen formulations of various dilutions against cat flea in egg, larval and adult stages when the subject product, which is a manufacturing use concentrate, is used to prepare end use products. Specific claims are dependent upon concentration, frequency of application and various other factors which are beyond the scope of this review and will need to be handled on an individual case-by-case basis. It will be necessary for either the registrant or their customers who purchase this product for use in formulating their own end use products to provide labeling outlining the types of claims which are applicable to their formulation(s).--RL Vern L. McFarland, IB"

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on

Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298501. Miller, T. 2003. Effect of Shampoo After Treatment with Cyphenothrin Squeeze-on on Efficacy against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Ticks (*Rhipicephalus sanguineus*) on Dogs: Analysis of Data and Conclusions. Project Number: MS/20D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 15 p.

A squeeze-on formulation containing cyphenothrin was applied once to two groups of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*) and ticks (*Rhipicephalus sanguineus*). The dose rate was 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. The treated dogs were bathed with low detergent shampoos 12 days after treatment and wetted with water on the 19th day. No significant effect of shampoo on the residual efficacy of the spot-on was observed. Efficacy, at 90% or better compared with untreated controls, was shown against fleas for up to 16 days and against ticks for 30 days. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitoes on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate and the formulation contains 2.3% s-Methoprene, which is not in the formulation of the registration being sought. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is >11.012 mg Cyphenothrin/kg, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

Data Support for 2517-ON

MRID 46039501. Cruthers, L. 2003. Efficacy Evaluation of a Permethrin Squeeze-On Against Adult Cat Fleas (*Ctenocephalides Felis*), Adult Brown Dog Ticks (*Rhipicephalus Sanguineus*), Nymphal Deer Ticks (*Ixodes Scapularis*) and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0243. Unpublished study prepared by Professional Laboratory and Research. 79 p.

The cited study was not applicable to the registration desired. The study examined the efficacy of 45% permethrin formulations against various pet parasites.

MRID 46039501 was not considered in support of the registration of 2517-ON.

MRID 46041303. Miller, T. 2003. Dose Titration of an S-Methoprene Spot-On (sic) Dogs: Final Report, Statistical Analyses and Conclusions. Unpublished study prepared in cooperation with Auburn University. 19 p.

The primary objective was to determine the dose rate of s-methoprene in a spot-on formulation that would provide one month of residual flea ovisterilant activity on dogs: Regression-correlation analyses showed that only when the dose rate was logarithmically transformed ($\log_N$ mg/kg) was there a highly significant correlation between dose rate and duration of residual flea ovisterilant efficacy at the 90% level. The resultant regression equation predicted that a dose rate of 2.8 mg/kg provides 30 days of efficacy at 90%. The correlation between dose rate and residual efficacy at the 100% level was not statistically significant. However, flea eggs collected on day 31 from the two cats treated at the highest dose rates of 3.5 to 3.6 mg/kg were all sterile, indicating that the predicted dose rate for a 100% residual efficacy claim is about these values.

The study dose rate (~3.5 mg/kg) and proposed dose rate (2.8 mg/kg) are 10x greater than the highest label dose rate(0.296 mg/kg). Thus, the study does not support the desired registration.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*,

and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitos on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is approximately > 1/10th the study dose rate, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

MRID ????????

ENTOMOLOGIST'S COMMENTS AND RECOMMENDATIONS:

Comment on the requirement for an animal safety study is deferred to the risk and product managers.

The cited data do not support the desired registrations because the study dose rates are above the label application rates. It is not possible to bridge these data to support the desired efficacy claims against fleas, ticks, or mosquitoes. Claims related to product efficacy have not been addressed below, but will be if the registrant is able to submit or cite relevant efficacy data, the following general label comments apply.

Remove control claims throughout the labels. The product will provide relief from the pests for the supported duration, but will not offer control of pests.

Label Comments:

2517-IN Claims:

[MASTERCARTON/PACK LABEL - FRONT PANEL]

1. Pleasant Fresh Scent [or] [Fragrance]]
2. ~~Flea & Tick Control for Dogs & Puppies 12 weeks old and older~~
3. ?? {?? - dependent on applicator size and quantity in market package - "e.g. 3, 6 or 12 Months"} Supply][For Dogs Weighing Up To ?? Lbs.]*
4. ~~Five Way Protection~~ [Kills fleas, ticks, mosquitoes, flea eggs & larvae] [for up to 42 days] [per application]*
5. ~~Five Way Protection to~~ [Kills fleas, ticks, mosquitoes, flea eggs & larvae]
6. ~~Five Way Protection!~~ Kills ticks, mosquitoes, fleas, flea eggs & larvae]
7. ~~5 Way Protection!~~ Kills ticks, mosquitoes, fleas, flea eggs & larvae
8. Extended Protection [[42-Day] [6 Week] Flea ,Tick & Mosquito Treatment]*
9. 42-Day Flea and Tick ~~Control~~*
10. With Nylar® Insect Growth Regulator which Breaks the Flea Life Cycle
11. With Nylar® to Break Flea Life Cycle*
12. With Insect Growth Regulator to Break Flea Life Cycle*
13. Dual Action[!] Cyphenothrin with Nylar® IGR Effectively Breaks the Flea Life Cycle
14. Dual Action [!]: Effectively Breaks the Flea Life Cycle[!]*
15. [For Dogs & Puppies (Over 12 Weeks of Age) Less than 15 lbs.]
16. [For Dogs & Puppies (Over 12 Weeks of Age) 15 to 33 lbs.]
17. [For Dogs & Puppies (Over 12 Weeks of Age) 33 to 66 lbs.]
18. [For Dogs & Puppies (Over 12 Weeks of Age) 66 lbs and Over]
19. Three Applications {for cartons with 3 applicators}.] and for [4-1/2 Month Supply] or [18 Week Supply]
20. For Dogs [less than 15 lbs.] or [15 lbs. to 33 lbs.] or [33 lbs. to 66 lbs.] or [66 lbs. and Over]
21. Breaks Flea Life Cycle!*
22. Best if used year round!
23. Kills & Repels Fleas Up to [6 weeks], [42 days]!*
24. ~~Kills & Repels New Fleas in less than 1 hour!*~~
25. ~~Kills & Repels New Ticks in less than 3 hours!*~~
26. ~~Kills & Repels 95% of Fleas and Ticks [and continues to work for up to six weeks]~~
27. ~~Kills 99% of Fleas one day after application~~
28. ~~Prevents ticks from attaching and feeding within 3 hours after application~~
29. ~~95% efficacy against ticks for up to[6 weeks] [42 days]~~
30. ~~Kills and Detaches Ticks~~
31. Kills over 95% of Ticks
32. Easy to Use Application
33. Specially Formulated for Dogs and Puppies
34. 42 Day Protection!
35. Monthly Calendar Stickers Inside!
36. ~~Patented Technology [combines effectiveness with gentleness!]~~
37. Kills Flea Eggs & Larvae for more than [63 days], [9 weeks]!*
38. Prevents Flea Eggs From Developing Into Biting Adults*

39. Kills Mosquitoes for up to [30 days!] [42 days!]*
40. Kills Mosquitoes ~~(vector of West Nile Virus)~~ for up to [30 days][42 days!]*
41. Protects Against Blood Feeding by Mosquitoes (that may [transmit][carry][vector] of Heartworm) For up to [30 days!] [42 days!]*
42. Kills & Repels Ticks for Up to [42 days], [6 weeks] !*
43. Kills & Repels Deer Ticks (vector of Lyme Disease) for up to [35 days!] [42 days!]*
44. Kills & Repels Ticks (Including Deer Ticks) for up to [35 days!][42 days!]*
45. Kills & Repels Brown Dog Ticks [(*Rhipicephalus sanguineus*)] for up to 42 days!]*
46. Kills & Repels American Dog Ticks [(*Dermacentor variabilis*)] or up to 42 days!*
47. Apply every [42 days], [6 weeks]!*
48. 42 Days Flea and Tick Treatment!*
49. Kills & Repels Fleas and Ticks for up to 42 days!*
50. Kills all stages of the flea life cycle*
51. Kills Fleas, Flea Eggs & Larvae for up to 6 Weeks*
52. ~~Kills & repels mosquitoes that are may [transmit][carry][be vectors] of West Nile Virus.]~~
53. Waterproof formula.
54. Dogs can be bathed 24 hours after squeeze-on is applied]
55. ~~Continues to work 50% longer than other leading brands~~
56. ~~Longest lasting, quick acting~~
57. *[MASTERCARTON/PACK LABEL – BACK/SIDE PANNELS CON'T]*

[Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] is an effective and easy to use product.] [Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] has demonstrated ~~greater than 95%~~ control of fleas and ticks within one day of application.] [Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] prevents eggs from fleas on treated dogs from developing into biting adults for 63 days.] [As with all flea and tick control products, Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] should be used as part of a [an overall] [complete] program [aimed at] [to] [intended to] [reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

2517-ON Claims:

[CARTON LABEL - DRAFT MASTER LABEL COPY]

1. Pleasant Fresh Scent [or][Fragrance]
2. Flea & Tick Control for Dogs & Puppies 12 weeks old and older][18 week], [24],[36], [48][54] [72] Week Supply For Dogs weighing [less than 15 lbs], [15 to 33 lbs], [33 to 66 lbs] [66 lbs and over] [15 lbs and over]*
3. Four Way Protection [Kills [fleas] and [ticks], [for up to six weeks], [flea eggs] [for up to one month]] and prevents mosquitoes from feeding on dogs [for up to three weeks!]
4. Works up to [6] [Six] Weeks on fleas and ticks!]
5. Protects for up to [6] [Six] Weeks against [fleas] [ticks]!]
6. Kills [For Up To 6 Weeks:] fleas and ticks, [For up to 6 Weeks] and-prevents mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile Virus)~~ from feeding on dogs for up to three weeks!
7. Kills Flea eggs for up to one month
8. ~~Four Way Protection~~ Kills fleas, ticks, and flea eggs and prevents mosquitoes from feeding on dogs]*
9. ~~Four Way Protection!~~ Kills fleas, ticks, and flea eggs and prevents mosquitoes from feeding on dogs]*
10. ~~4 Way Protection! Kills fleas, ticks, and flea eggs and prevents mosquitoes from feeding on dogs]*~~
11. ~~[Extended Protection] 4 Way Protection7 [4 Way Extended Protection] [[42 Day] [6 Week] [Flea & Tick Treatment]*~~
12. 42-Day Flea [Six (6) Week] [Flea and Tick Control]*
13. Prevents mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile Virus)~~ from feeding on dogs for up to 3 weeks]
14. With methoprene an Insect Growth Regulator which Breaks the Flea Life Cycle*
15. With methoprene to Break Flea Life Cycle*
16. With Insect Growth Regulator to Break Flea Life Cycle*
17. Dual Action [!]: Cyphenothrin with methoprene IGR Effectively Breaks the Flea Life Cycle] *
18. Dual Action [!]: Effectively Breaks the Flea Life Cycle[!]*
19. For Dogs & Puppies (Over 12 Weeks of Age) Less than 15 lbs.][* For Dogs & Puppies (Over 12 Weeks of Age) 15 to 33 lbs.][* For Dogs & Puppies (Over 12 Weeks of Age) 33 to 66 lbs.][* For Dogs & Puppies (Over 12 Weeks of Age) 66 lbs and Over]
20. Three Applications {for cartons with 3 applicators} and or [4-1/2 Month Supply] or [18 Week Supply]
21. For Dogs [less than 15 lbs.] or [15 lbs. to 33 lbs.] or [33 lbs. to 66 lbs.] or [66 lbs. and Over]
22. Breaks Flea Life Cycle!*
23. Best if used year round!
24. Kills & Repels Fleas Up to [6 weeks], [42 days]!*
25. ~~Kills & Repels New Fleas in less than 1 hour!*~~
26. ~~Kills & Repels New Ticks in less than 3 hours!*~~
27. ~~Kills & Repels 95% of Fleas and Ticks [and continues to work for up to six weeks]~~

28. ~~Kills 100% of Fleas on first day after application~~
29. ~~Kills 100% of Fleas on Day One!~~
30. ~~Kills 100% of Fleas and Ticks on Day Two!~~
31. ~~Kills 100% of Fleas and Ticks on the second day after application.~~
32. ~~Kills 100% of Fleas in first [24 Hours] [Day]!~~
33. ~~Kills 100% of Fleas and Ticks in [48 Hours] [2 Days]!~~
34. ~~Prevents ticks from attaching and feeding within 3 hours after application~~
35. ~~95% efficacy against ticks for up to [6 weeks] [42 days]~~
36. ~~Kills and Detaches Ticks~~
37. ~~Kills over 95% of Ticks~~
38. Easy to Use Application
39. Specially Formulated for Dogs and Puppies
40. 42 Day Protection against fleas and ticks!
41. 21 Day Protection against mosquitoes!
42. Reminder Calendar Stickers Inside!
43. ~~Patented Technology [combines effectiveness with gentleness!]~~
44. Kills Flea Eggs for 30 days]
45. Prevents Flea Eggs From Developing Into Biting Adults*
46. Prevents mosquitoes from feeding on dogs for up to [21 days!]
47. Prevents mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile Virus)~~ from feeding on dogs for up to [21 days]*
48. Protects Against Blood Feeding by Mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile virus)~~ For up to [21 days!]*
49. Kills & Repels Ticks for Up to [42 days],[6 weeks]!]*
50. Kills & Repels Deer Ticks (that may [transmit][carry][be a vector] of Lyme Disease) for up to [35 days!] [42 days!]*
51. Kills & Repels Ticks (Including Deer Ticks) for up to [35 days!] [42 days!]*
52. Kills & Repels Brown Dog Ticks [(*Rhipicephalus sanguineus*)] for up to 42 days!*
53. Kills & Repels American Dog Ticks [(*Dermacentor variabilis*)] for up to 42 days!*
54. Apply once every [42 days], [6 weeks]!*
55. 42 Days Flea and Tick Treatment!*
56. Kills & Repels Fleas and Ticks for up to 42 days!*
57. Kills Fleas and Flea Eggs for up to 4 Weeks*
58. ~~Prevents mosquitoes that are vectors of West Nile virus from feeding on dogs.~~
59. ~~Continues to work 50% longer than other leading brand.~~
60. ~~Longest lasting, quick acting]~~
61. ~~Kills [& Repels] [for Six [6] Weeks] [New] Fleas [in 1 hour], and [new] ticks [in 3 hours] [for up to 6 weeks]~~
62. *[BACK/SIDE CARTON LABEL - MASTER LABEL]*

[Sergeant's Squeeze-On Flea & Tick Control with methoprene is an effective and easy to use product.] [Sergeant's Squeeze-On Flea & Tick Control with methoprene has demonstrated greater than 95% of fleas and ticks within one day of application.] [Sergeant's Squeeze-On Flea & Tick Control with methoprene prevents eggs from fleas on treated dogs from developing into biting adults for 30 days.] [As with all flea and tick control products, Sergeant's Squeeze-On Flea and Tick Control with

PRODUCT PERFORMANCE / EFFICACY REVIEW
Mark Suarez, Entomologist - 1B

DATE:	26 September 2006
EPA REG. NUMBER:	2517-IN 2517-ON
PRODUCT NAME:	Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [**2517-IN**] Sergeant's Cyphenothrin + Methoprene Squeeze-On for Dogs [**2517-ON**]
REGISTRANT:	Sergeant's Pet Care Products, Inc.
PM: **REVIEWER:**	George LaRocca, PM13 Linda DeLuise
DECISION #.:	338118 [**2517-IN**] 358246 [**2517-ON**]
DP BARCODE:	305945 [**2517-IN**] 307614 " 319065 [**2517-ON**]
ACTION:	R31 [**2517-IN**] R26 [**2517-ON**]
ACTIVE INGREDIENT(S):	129013, Cyphenothrin.....40.0% [**2517-IN**] 129032, Pyriproxyfen.....2.0% 129013, Cyphenothrin.....40.0% [**2517-ON**] 105402, s-Methoprene.....2.3%
TYPE:	Wipe-On (Squeeze-On) for Dogs
OPPTS GUIDELINE(S):	810.1000 810.3000 810.3300
MRID:	46346601 46039501 46041303 46166109 46298501 46298502 42614501 45086801

MRIDs [cont.]	44948301 44546601
GLP ?:	No.
SITES:	Dogs; Puppies (≥12 weeks old)
PESTS:	Fleas (adult); Fleas (eggs); Fleas (larvae); Ticks; Mosquitoes; Mosquitoes (vector of WNV); Mosquitoes (vector of Heartworm); Deer Ticks (vector of Lyme Disease)
STUDY APPLICATION RATE:	variable (generally 100 mg AI/kg)
LABEL APPLICATION RATE:	Cyphenothrin: <15 kg: 1.0mL (>3.43 mg AI/kg)* 15-33kg: 1.5mL (2.38 – 5.14 mg AI/kg) 33-66kg: 3.0mL (2.34 – 4.68 mg AI/kg) >66kg: 4.5mL (<3.51 mg AI/kg) Pyriproxyfen: <15 kg: 1.0mL (>0.171 mg AI/kg)* 15-33kg: 1.5mL (0.117 – 0.257 mg AI/kg) 33-66kg: 3.0mL (0.117 – 0.234 mg AI/kg) >66kg: 4.5mL (<0.175 mg AI/kg) s-Methoprene: <15 kg: 1.0mL (>0.197 mg AI/kg)* 15-33kg: 1.5mL (0.134 – 0.296 mg AI/kg) 33-66kg: 3.0mL (0.134 – 0.269 mg AI/kg) >66kg: 4.5mL (<0.202 mg AI/kg)

* 40% Cypermethrin w/w, 2.0% Pyriproxyfen w/w, 2.3% s-Methoprene w/w; Specific Gravity of the formulation = 1.073 lb/gal

STUDY SUMMARIES:

The registrant submitted and cited a number of studies in support of two new cyphenothrin-based squeeze-on products for the protection of dogs against fleas, ticks, and mosquitoes. Each of these products contains the adulticide cyphenothrin, in addition to an insect growth regulator (IGR). In the case of 2517-IN, the IGR is pyriproxyfen (i.e., Nylar®); in 2517-ON the IGR is s-Methoprene. The incorporation of an IGR is expected to enhance the effectiveness of the product by negatively affecting the development of immature stages of fleas.

Data Support for 2517-IN

MRID 42684501. Rogosheske, S. 1990. Residual Effectiveness of Nylar on Cat Flea Larvae as a Carpet/Premise Spray: Lab Project Number: F-0122-90. Unpublished study prepared by McLaughlin Gormley King Co. 16 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN.

MRID 44546601. Anderson, K.; Solberg, J. 1998. Product Performance/Efficacy Reports: Evercide Pet and Plant Spray 2648: Lab Project Number: E-3459-97: 10-223-1085: 10-223-1185. Unpublished study prepared by McLaughlin Gormley King Co. 120 p.

From DER dated 27 June 2000 [No electronic copy available; these are the conclusions]:

"The data presented in EPA Accession (MRID) Number 44546601, having been obtained from standard laboratory and kennel testing conducted according to requirements of 95-9(a) subpart (1)-(3) on p. 263 and meeting the standards of 95-9(b)(2)(i) on p. 264 of the Product Performance Guidelines, are adequate to support the claims for killing adult fleas on contact by direct spray as summarized under Tab A in the previously mentioned volume, where a similar formulation was sprayed into a plastic pail onto *CTENOCEPHALIDES FELIS* adults on white terry cloth at 2 different area rates with 99% mortality in both cases. In a similar manner, the data summarized under Tab B in the volume are adequate to support the claims for killing ticks on contact by direct spray, where the same similar formulation is sprayed onto *RHIPICEPHALUS SANGUINEUS* on filter paper in a glass crystallizing dish with the result that 100% mortality occurred at a standard dosage of 1.0 ml. Additionally, data summarized under Tab C of the volume are adequate to support the claims for killing of fleas for 14 days and ticks for up to 7 days following trigger spray or pump spray application of a similar formulation (with lower concentration of active ingredients) to dogs of mixed sexes and weights and haircoat length as well as breeds at a rate sufficient to wet the coat to saturation, with the result that cat flea mortality was maintained at 100% for 14 days and mortality of American dog tick, *DERMACENTOR VARIABILIS*, was 100% at 3 days but fell to a marginally acceptable 81% at 7 days. Furthermore, data summarized under Tab d of the volume are adequate to support the claims for killing of fleas for 23 days and ticks for 9 days following trigger spray or pump spray application of the same similar formulation as in Tab C to cats of mixed sexes and haircoat length as well as weights at an average rate of 10.75 grams product per kilogram of pet body weight, with the result that cat flea mortality was maintained at 93% or above for 23 days and mortality of brown dog tick was maintained at or above 92% for 9 days. We will accept a claim for rapid knockdown and kill of fleas on dogs following application of the subject product at a rate sufficient to saturate the animal's coat, based on the fact that that the similar

formulation resulted in 100% mortality of cat fleas at 1 hour after spraying. Finally, we will accept the claim for killing [controlling] deer ticks and other ticks [Ixodid] species that may carry and transmit Lyme disease, on the basis of the fact that both the American dog tick and the brown dog tick are Ixodid ticks plus we have previously accepted similar formulations of permethrin and pyrethrins in combination that were effective against deer tick. -- RL Vern L. McFarland, IB"

The cited MRID could not be considered in support of the subject formulations because the test formulations were not similar to those under consideration. The test formulations contained permethrin and pyrethrins, not cyphenothrin, pyriproxyfen, or s-methoprene.

MRID 44948301. Schlekau, J. 1999. Product Performance/Efficacy Reports: Nylar Concentrate 2607: Lab Project Number: TL-3095: TL-3096: TL-3097. Unpublished study prepared by McLaughlin Gormley King Co. 61 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with a shampoo or direct spray containing pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence and notable residual activity for the duration of the study (>90, for 6 to 13 months) months, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN.

MRID 45086801. Donahue, W.; Meola, S.; Palma, K. et al. 2000. Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.

From DER dated 27 June 2000:

"CONCLUSIONS & RECOMMENDATIONS The data presented in EPA Accession (MRID) Number 450868-01, having been compiled from standard laboratory and kennel testing conducted according to requirements of § 95-9(a)(1) to (3) on p. 263 and meeting the standard of § 95-9, subpart (b)(2)(i) on p. 264 of the Product Performance Guidelines are adequate to support claims of inhibiting the hatch of larval fleas, killing of flea eggs, inhibiting the hatch of flea eggs and adversely affecting the physiological health of fleas when the subject product is diluted to produce end use products having a active ingredient [pyriproxyfen] concentration of 0.01% and 0.025% as a dip and 0.025% and 0.05% as a shampoo in the testing reported in the portion under Tab 1; are adequate to demonstrate the physiological effects of extremely low concentrations of active ingredient on the molecular structure of flea eggs exposed to pyriproxyfen in glass vials having a deposit of 0.25 mg/cm^2 as reported in the portion under Tab 2, to the extent that pyriproxyfen prevented cellular differentiation and no blastoderm had formed in eggs that were collected even more than 50 hours after exposure; are adequate to demonstrate the inhibition of egg hatch and emergence of adult fleas when eggs were exposed to either

residues of 1.1 mg/cm^2 on filter paper or the same deposit on aliquots of dog hair, which were prepared by using a standard dilution of 0.007% a.i. solution, or when exposed to dog hair that had been treated with pyriproxyfen as a 0.125% spray, all of which were reported under Tab 3; and are adequate to demonstrate the following physiological effects on adults and eggs of the cat flea, *Ctenocephalides felis*, when adult fleas of both sexes were exposed to 1.1 mg AI/cm^2 on treated filter paper: histological studies of unfed fleas demonstrated that pyriproxyfen exposure caused depletion of fat body reserves and death by starvation, and fed fleas exposed to pyriproxyfen-treated dog hair also appeared to die of starvation, while eggs deposited by females in these tests were largely empty shells; additionally, studies on flea eggs suggested that pyriproxyfen was less effective as an ovicide than fenoxycarb, that pyriproxyfen exposure of newly laid eggs did not prevent hatching, but 10 minute exposure of the eggs killed 50% of fleas that developed to larval stage. These new findings, all of which were reported under Tab 4, indicated that pyriproxyfen had an unusual latent effect in which short-term exposure of flea eggs early in embryogenesis was often lethal to flea larvae that hatched from the egg 3 days later. In contrast, a longer-term (2-hour) exposure of eggs to pyriproxyfen produced embryocidal effects. Thus, these data are collectively adequate to demonstrate the effectiveness of pyriproxyfen formulations of various dilutions against cat flea in egg, larval and adult stages when the subject product, which is a manufacturing use concentrate, is used to prepare end use products. Specific claims are dependent upon concentration, frequency of application and various other factors which are beyond the scope of this review and will need to be handled on an individual case-by-case basis. It will be necessary for either the registrant or their customers who purchase this product for use in formulating their own end use products to provide labeling outlining the types of claims which are applicable to their formulation(s).--RL Vern L. McFarland, IB"

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on

Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298501. Miller, T. 2003. Effect of Shampoo After Treatment with Cyphenothrin Squeeze-on on Efficacy against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Ticks (*Rhipicephalus sanguineus*) on Dogs: Analysis of Data and Conclusions. Project Number: MS/20D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 15 p.

A squeeze-on formulation containing cyphenothrin was applied once to two groups of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*) and ticks (*Rhipicephalus sanguineus*). The dose rate was 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. The treated dogs were bathed with low detergent shampoos 12 days after treatment and wetted with water on the 19th day. No significant effect of shampoo on the residual efficacy of the spot-on was observed. Efficacy, at 90% or better compared with untreated controls, was shown against fleas for up to 16 days and against ticks for 30 days. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitoes on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate and the formulation contains 2.3% s-Methoprene, which is not in the formulation of the registration being sought. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is >11.012 mg Cyphenothrin/kg, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

Data Support for 2517-ON

MRID 46039501. Cruthers, L. 2003. Efficacy Evaluation of a Permethrin Squeeze-On Against Adult Cat Fleas (*Ctenocephalides Felis*), Adult Brown Dog Ticks (*Rhipicephalus Sanguineus*), Nymphal Deer Ticks (*Ixodes Scapularis*) and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0243. Unpublished study prepared by Professional Laboratory and Research. 79 p.

The cited study was not applicable to the registration desired. The study examined the efficacy of 45% permethrin formulations against various pet parasites.

MRID 46039501 was not considered in support of the registration of 2517-ON.

MRID 46041303. Miller, T. 2003. Dose Titration of an S-Methoprene Spot-On (sic) Dogs: Final Report, Statistical Analyses and Conclusions. Unpublished study prepared in cooperation with Auburn University. 19 p.

The primary objective was to determine the dose rate of s-methoprene in a spot-on formulation that would provide one month of residual flea ovisterilant activity on dogs: Regression-correlation analyses showed that only when the dose rate was logarithmically transformed ($\log_N$ mg/kg) was there a highly significant correlation between dose rate and duration of residual flea ovisterilant efficacy at the 90% level. The resultant regression equation predicted that a dose rate of 2.8 mg/kg provides 30 days of efficacy at 90%. The correlation between dose rate and residual efficacy at the 100% level was not statistically significant. However, flea eggs collected on day 31 from the two cats treated at the highest dose rates of 3.5 to 3.6 mg/kg were all sterile, indicating that the predicted dose rate for a 100% residual efficacy claim is about these values.

The study dose rate (~3.5 mg/kg) and proposed dose rate (2.8 mg/kg) are 10x greater than the highest label dose rate(0.296 mg/kg). Thus, the study does not support the desired registration.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*,

and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitos on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is approximately > 1/10th the study dose rate, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

MRID ????????

ENTOMOLOGIST'S COMMENTS AND RECOMMENDATIONS:

Comment on the requirement for an animal safety study is deferred to the risk and product managers.

The cited data do not support the desired registrations because the study dose rates are above the label application rates. It is not possible to bridge these data to support the desired efficacy claims against fleas, ticks, or mosquitoes. Claims related to product efficacy have not been addressed below, but will be if the registrant is able to submit or cite relevant efficacy data, the following general label comments apply.

Remove control claims throughout the labels. The product will provide relief from the pests for the supported duration, but will not offer control of pests.

Label Comments:

2517-IN Claims:

[MASTERCARTON/PACK LABEL - FRONT PANEL]

1. Pleasant Fresh Scent [or] [Fragrance]]
2. ~~Flea & Tick Control for Dogs & Puppies 12 weeks old and older~~
3. ?? {?? - dependent on applicator size and quantity in market package - "e.g. 3, 6 or 12 Months"} Supply][For Dogs Weighing Up To ?? Lbs.]*
4. ~~Five Way Protection~~ [Kills fleas, ticks, mosquitoes, flea eggs & larvae] [for up to 42 days] [per application]*
5. ~~Five Way Protection to~~ [Kills fleas, ticks, mosquitoes, flea eggs & larvae]
6. ~~Five Way Protection!~~ Kills ticks, mosquitoes, fleas, flea eggs & larvae]
7. ~~5 Way Protection!~~ Kills ticks, mosquitoes, fleas, flea eggs & larvae
8. Extended Protection [[42-Day] [6 Week] Flea ,Tick & Mosquito Treatment]*
9. 42-Day Flea and Tick ~~Control~~*
10. With Nylar® Insect Growth Regulator which Breaks the Flea Life Cycle
11. With Nylar® to Break Flea Life Cycle*
12. With Insect Growth Regulator to Break Flea Life Cycle*
13. Dual Action[!] Cyphenothrin with Nylar® IGR Effectively Breaks the Flea Life Cycle
14. Dual Action [!]: Effectively Breaks the Flea Life Cycle[!]*
15. [For Dogs & Puppies (Over 12 Weeks of Age) Less than 15 lbs.]
16. [For Dogs & Puppies (Over 12 Weeks of Age) 15 to 33 lbs.]
17. [For Dogs & Puppies (Over 12 Weeks of Age) 33 to 66 lbs.]
18. [For Dogs & Puppies (Over 12 Weeks of Age) 66 lbs and Over]
19. Three Applications {for cartons with 3 applicators}.] and for [4-1/2 Month Supply] or [18 Week Supply]
20. For Dogs [less than 15 lbs.] or [15 lbs. to 33 lbs.] or [33 lbs. to 66 lbs.] or [66 lbs. and Over]
21. Breaks Flea Life Cycle!*
22. Best if used year round!
23. Kills & Repels Fleas Up to [6 weeks], [42 days]!*
24. ~~Kills & Repels New Fleas in less than 1 hour!*~~
25. ~~Kills & Repels New Ticks in less than 3 hours!*~~
26. ~~Kills & Repels 95% of Fleas and Ticks [and continues to work for up to six weeks!]~~
27. ~~Kills 99% of Fleas one day after application~~
28. ~~Prevents ticks from attaching and feeding within 3 hours after application~~
29. ~~95% efficacy against ticks for up to[6 weeks] [42 days]~~
30. ~~Kills and Detaches Ticks~~
31. Kills over 95% of Ticks
32. Easy to Use Application
33. Specially Formulated for Dogs and Puppies
34. 42 Day Protection!
35. Monthly Calendar Stickers Inside!
36. ~~Patented Technology [combines effectiveness with gentleness!]~~
37. Kills Flea Eggs & Larvae for more than [63 days], [9 weeks]!*
38. Prevents Flea Eggs From Developing Into Biting Adults*

39. Kills Mosquitoes for up to [30 days!] [42 days!]*
40. Kills Mosquitoes ~~(vector of West Nile Virus)~~ for up to [30 days][42 days!]*
41. Protects Against Blood Feeding by Mosquitoes (that may [transmit][carry][vector] of Heartworm) For up to [30 days!] [42 days!]*
42. Kills & Repels Ticks for Up to [42 days], [6 weeks] !*
43. Kills & Repels Deer Ticks (vector of Lyme Disease) for up to [35 days!] [42 days!]*
44. Kills & Repels Ticks (Including Deer Ticks) for up to [35 days!][42 days!]*
45. Kills & Repels Brown Dog Ticks [(*Rhipicephalus sanguineus*)] for up to 42 days!]*
46. Kills & Repels American Dog Ticks [(*Dermacentor variabilis*)] or up to 42 days!*
47. Apply every [42 days], [6 weeks]!*
48. 42 Days Flea and Tick Treatment!*
49. Kills & Repels Fleas and Ticks for up to 42 days!*
50. Kills all stages of the flea life cycle*
51. Kills Fleas, Flea Eggs & Larvae for up to 6 Weeks*
52. ~~Kills & repels mosquitoes that are~~ ~~may [transmit][carry][be vectors]~~ ~~of West Nile Virus.]~~
53. Waterproof formula.
54. Dogs can be bathed 24 hours after squeeze-on is applied]
55. ~~Continues to work 50% longer than other leading brands~~
56. ~~Longest-lasting, quick-acting~~
57. *[MASTERCARTON/PACK LABEL – BACK/SIDE PANNELS CON'T]*

[Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] is an effective and easy to use product.] [Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] has demonstrated ~~greater than 95%~~ control of fleas and ticks within one day of application.] [Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] prevents eggs from fleas on treated dogs from developing into biting adults for 63 days.] [As with all flea and tick control products, Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [with] [Nylar®] [an] [Insect Growth Regulator] should be used as part of a [an overall] [complete] program [aimed at] [to] [intended to] [reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

2517-ON Claims:

[CARTON LABEL - DRAFT MASTER LABEL COPY]

1. Pleasant Fresh Scent [or][Fragrance]
2. Flea & Tick Control for Dogs & Puppies 12 weeks old and older][18 week], [24],[36], [48][54] [72] Week Supply For Dogs weighing [less than 15 lbs], [15 to 33 lbs], [33 to 66 lbs] [66 lbs and over] [15 lbs and over]*
3. Four Way Protection [Kills [fleas] and [ticks], [for up to six weeks], [flea eggs] [for up to one month]] and prevents mosquitoes from feeding on dogs [for up to three weeks!]
4. Works up to [6] [Six] Weeks on fleas and ticks!]
5. Protects for up to [6] [Six] Weeks against [fleas] [ticks]!]
6. Kills [For Up To 6 Weeks:] fleas and ticks, [For up to 6 Weeks] and prevents mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile Virus)~~ from feeding on dogs for up to three weeks!
7. Kills Flea eggs for up to one month
8. ~~Four Way Protection~~ Kills fleas, ticks, and flea eggs and prevents mosquitoes from feeding on dogs]*
9. ~~Four Way Protection!~~ Kills fleas, ticks, and flea eggs and prevents mosquitoes from feeding on dogs]*
10. ~~4 Way Protection! Kills fleas, ticks, and flea eggs and prevents mosquitoes from feeding on dogs]*~~
11. ~~[Extended Protection] 4 Way Protection7 [4 Way Extended Protection] {[42 Day] [6 Week] [Flea & Tick Treatment]*~~
12. 42-Day Flea [Six (6) Week] [Flea and Tick Control]*
13. Prevents mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile Virus~~ from feeding on dogs for up to 3 weeks]
14. With methoprene an Insect Growth Regulator which Breaks the Flea Life Cycle*
15. With methoprene to Break Flea Life Cycle*
16. With Insect Growth Regulator to Break Flea Life Cycle*
17. Dual Action [!]: Cyphenothrin with methoprene IGR Effectively Breaks the Flea Life Cycle] *
18. Dual Action [!]: Effectively Breaks the Flea Life Cycle[!]*
19. For Dogs & Puppies (Over 12 Weeks of Age) Less than 15 lbs.][* For Dogs & Puppies (Over 12 Weeks of Age) 15 to 33 lbs.][* For Dogs & Puppies (Over 12 Weeks of Age) 33 to 66 lbs.][* For Dogs & Puppies (Over 12 Weeks of Age) 66 lbs and Over]
20. Three Applications {for cartons with 3 applicators} and or [4-1/2 Month Supply] or [18 Week Supply]
21. For Dogs [less than 15 lbs.] or [15 lbs. to 33 lbs.] or [33 lbs. to 66 lbs.] or [66 lbs. and Over]
22. Breaks Flea Life Cycle!*
23. Best if used year round!
24. Kills & Repels Fleas Up to [6 weeks], [42 days]!*
25. ~~Kills & Repels New Fleas in less than 1 hour!*~~
26. ~~Kills & Repels New Ticks in less than 3 hours!*~~
27. ~~Kills & Repels 95% of Fleas and Ticks [and continues to work for up to six weeks.]~~

28. ~~Kills 100% of Fleas on first day after application~~
29. ~~Kills 100% of Fleas on Day One!~~
30. ~~Kills 100% of Fleas and Ticks on Day Two!~~
31. ~~Kills 100% of Fleas and Ticks on the second day after application.~~
32. ~~Kills 100% of Fleas in first [24 Hours] [Day]!~~
33. ~~Kills 100% of Fleas and Ticks in [48 Hours] [2 Days]!~~
34. ~~Prevents ticks from attaching and feeding within 3 hours after application~~
35. ~~95% efficacy against ticks for up to [6 weeks] [42 days]~~
36. ~~Kills and Detaches Ticks~~
37. ~~Kills over 95% of Ticks~~
38. Easy to Use Application
39. Specially Formulated for Dogs and Puppies
40. 42 Day Protection against fleas and ticks!
41. 21 Day Protection against mosquitoes!
42. Reminder Calendar Stickers Inside!
43. ~~Patented Technology [combines effectiveness with gentleness!]~~
44. Kills Flea Eggs for 30 days]
45. Prevents Flea Eggs From Developing Into Biting Adults*
46. Prevents mosquitoes from feeding on dogs for up to [21 days!]
47. Prevents mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile Virus)~~ from feeding on dogs for up to [21 days]*
48. Protects Against Blood Feeding by Mosquitoes ~~(that may [carry][transmit][be vectors] of West Nile virus)~~ For up to [21 days!]*
49. Kills & Repels Ticks for Up to [42 days],[6 weeks]!]*
50. Kills & Repels Deer Ticks (that may [transmit][carry][be a vector] of Lyme Disease) for up to [35 days!] [42 days!]*
51. Kills & Repels Ticks (Including Deer Ticks) for up to [35 days!] [42 days!]*
52. Kills & Repels Brown Dog Ticks [(*Rhipicephalus sanguineus*)] for up to 42 days!*
53. Kills & Repels American Dog Ticks [(*Dermacentor variabilis*)] for up to 42 days!*
54. Apply once every [42 days], [6 weeks]!*
55. 42 Days Flea and Tick Treatment!*
56. Kills & Repels Fleas and Ticks for up to 42 days!*
57. Kills Fleas and Flea Eggs for up to 4 Weeks*
58. ~~Prevents mosquitoes that are vectors of West Nile virus from feeding on dogs.~~
59. ~~Continues to work 50% longer than other leading brand.~~
60. ~~Longest lasting, quick acting]~~
61. ~~Kills [& Repels] [for Six [6] Weeks] [New.] Fleas [in 1 hour], and [new] ticks [in 3 hours] [for up to 6 weeks]~~
62. *[BACK/SIDE CARTON LABEL - MASTER LABEL]*

[Sergeant's Squeeze-On Flea & Tick Control with methoprene is an effective and easy to use product.] [Sergeant's Squeeze-On Flea & Tick Control with methoprene has demonstrated greater than 95% of fleas and ticks within one day of application.] [Sergeant's Squeeze-On Flea & Tick Control with methoprene prevents eggs from fleas on treated dogs from developing into biting adults for 30 days.] [As with all flea and tick control products, Sergeant's Squeeze-On Flea and Tick Control with

methoprene should be used as part of a program aimed at reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

Enclosure
002517-0001N.-ON 2006SEP26

PRODUCT PERFORMANCE / EFFICACY REVIEW
Mark Suarez, Entomologist - IB

DATE:	7 November 2006
EPA REG. NUMBER:	2517-IL 2517-IN 2517-ON
PRODUCT NAME:	Sergeant's Cyphenothrin Squeeze-On for Dogs [**2517-IL**] Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [**2517-IN**] Sergeant's Cyphenothrin + Methoprene Squeeze-On for Dogs [**2517-ON**]
REGISTRANT:	Sergeant's Pet Care Products, Inc.
PM: **REVIEWER:**	George LaRocca, PM13 Linda DeLuise
DECISION #.:	345654 [**2517-IL**] 338118 [**2517-IN**] 358246 [**2517-ON**]
DP BARCODE:	305952 [**2517-IL**] 305945 [**2517-IN**] 307614 " 319065 [**2517-ON**]
ACTION:	R26 [**2517-IL**] R31 [**2517-IN**] R26 [**2517-ON**]
ACTIVE INGREDIENT(S):	129013, Cyphenothrin.....40.0% [**2517-IL**] 129013, Cyphenothrin.....40.0% [**2517-IN**] 129032, Pyriproxyfen.....2.0% 129013, Cyphenothrin.....40.0% [**2517-ON**] 105402, s-Methoprene.....2.3%
TYPE:	Wipe-On (Squeeze-On) for Dogs
OPPTS GUIDELINE(S):	810.1000 810.3000 810.3300

MRID:	46346601 46039501 46041303 46166109 46298501 46298502 42614501 45086801 44948301 44546601 46166110
GLP ?:	No.
SITES:	Dogs; Puppies (≥12 weeks old)
PESTS:	Fleas (adult); Fleas (eggs); Fleas (larvae); Ticks; Mosquitoes; Mosquitoes (vector of WNV); Mosquitoes (vector of Heartworm); Deer Ticks (vector of Lyme Disease)
STUDY APPLICATION RATE:	variable (generally 100 mg AI/kg)
LABEL APPLICATION RATE:	Cyphenothrin [All products]: >50 mgCyphenothrin per kg dog body weight for dogs <100 lbs Pyriproxyfen [2517-IN]: >2.5 mgCyphenothrin per kg dog body weight for dogs <100 lbs s-Methoprene [2517-ON]: >2.875 mg Cyphenothrin per kg dog body weight for dogs <100 lbs

STUDY SUMMARIES:

The registrant submitted and cited a number of studies in support of three new cyphenothrin-based squeeze-on products for the protection of dogs against fleas, ticks, and mosquitoes. Each of these products contains the adulticide cyphenothrin. In addition two of the formulations [2517-IN & 2517-ON] contain an insect growth regulator (IGR). In the case of 2517-IN, the IGR is pyriproxyfen (i.e., Nylar®); in 2517-ON the IGR is s-Methoprene. The incorporation of an IGR is expected to enhance the effectiveness of the products by negatively affecting the development of immature stages of fleas.

Data Submtted in Support of Cyphenothrin Activity

MRID 46166110. Young, D. 2003. Dose Titration of a Cyphenothrin Squeeze-On against Adult Cat Fleas (*Ctenocephalides felis*), AdultBrown Dog Ticks (*Rhipicephalus sanguineus*) on Dogs. Unpublished study prepared by Thomas A. Miller, Veterinary Research and Regulatory Consultant. 23 p.

The submitted date examined the efficaciousness of two dose rates of cypermethrin against fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) when applied to dogs. The study compared the number of parasites found on test animals following a dose of 0, 25, or 100 mg/kg. Against fleas, the data demonstrate that cyphenothrin provides a greater than 90% reducting, relative to the control group mean, for up to 23 days at the 25 mg/kg rate and 35 days at the 100 mg/kg rate. For the brown dog tick, the data demonstrate that cyphenothrin provides a greater than 90% reducting, relative to the control group mean, for up to 30 days at the 25 mg/kg rate and 44 days at the 100 mg/kg rate. No data were provided for the label application rate of 50 mg/kg.

The study data support label claims of 23 days against fleas and 30 days against brown dog ticks. Because the label rate is twice the lowest dose tested and the data for the higher dose testedthe registrant has argued that the product is likely to kill or repel fleas for up to 28 days (4 weeks/1 month). Under the condition that confirmatory data (for fleas and an additional tick species) be submitted within 12 months, a claim of 28 days against fleas and ticks is acceptable.

MRID 44546601. Anderson, K.; Solberg, J. 1998. Product Performauce/Efficacy Reports: Evercide Pet and Plant Spray 2648: Lab Project Number: E-3459-97: 10-223-1085: 10-223-1185. Unpublished study prepared by McLaughlin Gormley King Co. 120 p.

From DER dated 27 June 2000 [No electronic copy available; these are the conclusions]:

"The data presented in EPA Accession (MRID) Number 44546601, having been obtained from standard laboratory and kennel testing conducted according to requirements of 95-9(a) subpart (1)-(3) on p. 263 and meeting the standards of 95-9(b)(2)(i) on p. 264 of the Product Performance Guidelines, are adequate to support the claims for killing adult fleas on contact by direct spray as summarized under Tab A in the previously mentioned volume, where a similar formulation was sprayed into a plastic pail

onto *CTENOCEPHALIDES FELIS* adults on white terry cloth at 2 different area rates with 99% mortality in both cases. In a similar manner, the data summarized under Tab B in the volume are adequate to support the claims for killing ticks on contact by direct spray, where the same similar formulation is sprayed onto *RHIPICEPHALUS SANGUINEUS* on filter paper in a glass crystallizing dish with the result that 100% mortality occurred at a standard dosage of 1.0 ml. Additionally, data summarized under Tab C of the volume are adequate to support the claims for killing of fleas for 14 days and ticks for up to 7 days following trigger spray or pump spray application of a similar formulation (with lower concentration of active ingredients) to dogs of mixed sexes and weights and haircoat length as well as breeds at a rate sufficient to wet the coat to saturation, with the result that cat flea mortality was maintained at 100% for 14 days and mortality of American dog tick, *DERMACENTOR VARIABILIS*, was 100% at 3 days but fell to a marginally acceptable 81% at 7 days. Furthermore, data summarized under Tab d of the volume are adequate to support the claims for killing of fleas for 23 days and ticks for 9 days following trigger spray or pump spray application of the same similar formulation as in Tab C to cats of mixed sexes and haircoat length as well as weights at an average rate of 10.75 grams product per kilogram of pet body weight, with the result that cat flea mortality was maintained at 93% or above for 23 days and mortality of brown dog tick was maintained at or above 92% for 9 days. We will accept a claim for rapid knockdown and kill of fleas on dogs following application of the subject product at a rate sufficient to saturate the animal's coat, based on the fact that that the similar formulation resulted in 100% mortality of cat fleas at 1 hour after spraying. Finally, we will accept the claim for killing [controlling] deer ticks and other ticks [Ixodid] species that may carry and transmit Lyme disease, on the basis of the fact that both the American dog tick and the brown dog tick are Ixodid ticks plus we have previously accepted similar formulations of permethrin and pyrethrins in combination that were effective against deer tick. -- RL Vern L. McFarland, IB"

The cited MRID could not be considered in support of the subject formulations because the test formulations were not similar to those under consideration. The test formulations contained permethrin and pyrethrins, not cyphenothrin, pyriproxyfen, or s-methoprene.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298501. Miller, T. 2003. Effect of Shampoo After Treatment with Cyphenothrin Squeeze-on on Efficacy against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Ticks (*Rhipicephalus sanguineus*) on Dogs: Analysis of Data and Conclusions. Project Number: MS/20D. Unpublisbed study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 15 p.

A squeeze-on formulation containing cyphenothrin was applied once to two groups of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*) and ticks (*Rhipicephalus sanguineus*). The dose rate was 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. The treated dogs were bathed with low detergent sbampoos 12 days after treatment and wetted with water on the 19th day. No significant effect of shampoo on the residual efficacy of the spot-on was observed. Efficacy, at 90% or better compared with untreated controls, was shown against fleas for up to 16 days and against ticks for 30 days. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitoes on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes

(*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate and the formulation contains 2.3% s-Methoprene, which is not in the formulation of the registration being sought. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is >11.012 mg Cyphenothrin/kg, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

MRID 46039501. Cruthers, L. 2003. Efficacy Evaluation of a Permethrin Squeeze-On Against Adult Cat Fleas (*Ctenocephalides Felis*), Adult Brown Dog Ticks (*Rhipicephalus Sanguineus*), Nymphal Deer Ticks (*Ixodes Scapularis*) and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0243. Unpublished study prepared by Professional Laboratory and Research. 79 p.

The cited study was not applicable to the registration desired. The study examined the efficacy of 45% permethrin formulations against various pet parasites.

MRID 46039501 was not considered in support of the registration of 2517-ON.

MRID 46166109. Cruthers, L. 2003. Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*), American Dog Ticks (*Dermacentor variabilis*), Nymphal Deer Ticks (*Ixodes scapularis*), and Adult *Aedes aegypti* Mosquitoes on Dogs. Project Number: 0307. Unpublished study prepared by Professional Laboratory and Research and Thomas A. Miller, 342 p.

When applied at a rate of 100 mg/kg, the tested Cyphenothrin Spot-on was greater than 90% effective (based on comb counts) against adult cat fleas, *Ctenocephalides felis*, and nearly 90% effective against American dog ticks, *Dermacentor variabilis*, between test days 3 and 30.

On Test Day 37, this formulation was only ~81% and ~75% effective against adult fleas and ticks. The efficacy against adult fleas was less than ~47% on Test Days 44 and 51 and less than ~ 69% effective against adult ticks at these same times.

On Test Day 7, this cyphenothrin spot-on formulation was 100% effective against adult fleas at 1, 2 and 3 hours post-infestation and ~83, 89, and 95% effective respectively, against adult American dog ticks at these same time points. The majority of the dead fleas and ticks were found in the pans beneath the dog cages at 1 hour post-infestation on Test Day 7.

Hair removed from dogs treated with this cyphenothrin spot-on formulation killed ~98% of the nymphal deer ticks on Test Day 10 and ~81% of the nymphal deer ticks on Test Day 38. This cyphenothrin spot-on formulation reduced the net percent mosquito landings by ~28%, 19% and 0% on Test Days 9, 30 and 51, respectively. Net percent

mosquito mortality (really dead + moribund) was ~96%, 100% and 0% on Test Days 9, 30 and 51, respectively and the net percent reduction in blood-feeding was ~91%, 83% and 6% on Test Days 9, 30 and 51, respectively.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg AI/kg. The label dose rate is >5.14mg AI/kg, except for dogs less than 0.5 kg. Thus, the study does not support the desired registration.

MRID 46298502. Miller, T. 2003. Competitive Efficacy Evaluation of a Cyphenothrin Spot-On Against Adult Cat Fleas (*Ctenocephalides felis*), Adult Brown Dog Ticks (*Rhipicephalus sanguineus*) and Against Feeding by *Aedes albopictus* and *Culex quinquefasciatus* Adult Mosquitos on Dogs. Project Number: MS13D. Unpublished study prepared by Sharp Veterinary Hospital and Vetoquinol N.A., Inc. 25 p.

Squeeze-on formulations containing cyphenothrin, fipronil, or phenothrin were applied once a group of dogs that were infested and were subsequently re-infested with adult fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*), and mosquitoes (*Aedes albopictus* and *Culex quinquefasciatus*). The dose rate was approximately 100 mg/kg. Flea and tick counts were performed at 1 and 2 days after treatment and at 1 and 2 or 3 days after re-infestation. Efficacy, at 90% or better compared with untreated controls, was shown against fleas and ticks for up to 37 days. For mosquitoes, feeding was reduced by >90%, compared to controls, through 22 DAT. The data appear to support claims against adult fleas for up to 30 days, if the dog is not washed or wetted.

The study dose rate is substantially greater than the label dose rate. The dose rate used in the study was 100 mg Cyphenothrin/kg. The label dose rate is approximately > 1/10th the study dose rate, except for dogs less than 1 kg. Thus, the study does not support the desired registration.

Data Submited in Support of Puriproxyfen Activity

MRID 42684501. Rogosheske, S. 1990. Residual Effectiveness of Nylar on Cat Flea Larvae as a Carpet/Premise Spray: Lab Project Number: F-0122-90. Unpublished study prepared by McLaughlin Gormley King Co. 16 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis*, larva were treated with pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN because the test protocol was fundamentally different from the desired use pattern.

MRID 44948301. Schlekau, J. 1999. Product Performance/Efficacy Reports: Nylar Concentrate 2607: Lab Project Number: TL-3095: TL-3096: TL-3097. Unpublished study prepared by McLaughlin Gormley King Co. 61 p.

In the cited study, carpet samples infested with cat flea, *Ctenocephalides felis,* larva were treated with a shampoo or direct spray containing pyriproxyfen (Nylar®). Although the application resulted in significant reduction in adult emergence and notable residual activity for the duration of the study (>90, for 6 to 13 months) months, the biology of the parasite is such that the study does not aid in determination of the effectiveness of a spot-on. (The eggs fall off the animal and larvae hatch on the ground. Thus, the length of egg exposure to treated animal hair may not be adequate for the IGR to demonstrate insecticidal activity.)

MRID 42684501 was not considered in support of the registration of 2517-IN because the test protocol was fundamentally different from the desired use pattern.

MRID 45086801. Donahue, W.; Meola, S.; Palma, K. et al. 2000. Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.

From DER dated 27 June 2000:

"CONCLUSIONS & RECOMMENDATIONS The data presented in EPA Accession (MRID) Number 450868-01, having been compiled from standard laboratory and kennel testing conducted according to requirements of § 95-9(a)(1) to (3) on p. 263 and meeting the standard of § 95-9, subpart (b)(2)(i) on p. 264 of the Product Performance Guidelines are adequate to support claims of inhibiting the hatch of larval fleas, killing of flea eggs, inhibiting the hatch of flea eggs and adversely affecting the physiological health of fleas when the subject product is diluted to produce end use products having a active ingredient [pyriproxyfen] concentration of 0.01% and 0.025% as a dip and 0.025% and 0.05% as a shampoo in the testing reported in the portion under Tab 1; are adequate to demonstrate the physiological effects of extremely low concentrations of active ingredient on the molecular structure of flea eggs exposed to pyriproxyfen in glass vials having a deposit of 0.25 mg/cm^2 as reported in the portion under Tab 2, to the extent that pyriproxyfen prevented cellular differentiation and no blastoderm had formed in eggs that were collected even more than 50 hours after exposure; are adequate to demonstrate the inhibition of egg hatch and emergence of adult fleas when eggs were exposed to either residues of 1.1 mg/cm^2 on filter paper or the same deposit on aliquots of dog hair, which were prepared by using a standard dilution of 0.007% a.i. solution, or when exposed to dog hair that had been treated with pyriproxyfen as a 0.125% spray, all of which were reported under Tab 3; and are adequate to demonstrate the following physiological effects on adults and eggs of the cat flea, *Ctenocephalides felis*, when adult fleas of both sexes were exposed to 1.1 mg AI/cm^2 on treated filter paper: histological studies of unfed fleas demonstrated that pyriproxyfen exposure caused depletion of fat body reserves and death by starvation, and fed fleas exposed to pyriproxyfen-treated dog hair also appeared to die of starvation, while eggs deposited by females in these tests were largely empty shells; additionally, studies on flea eggs suggested that pyriproxyfen was less effective as an ovicide than fenoxycarb, that pyriproxyfen exposure of newly laid eggs did not prevent

hatching, but 10 minute exposure of the eggs killed 50% of fleas that developed to larval stage. These new findings, all of which were reported under Tab 4, indicated that pyriproxyfen had an unusual latent effect in which short-term exposure of flea eggs early in embryogenesis was often lethal to flea larvae that hatched from the egg 3 days later. In contrast, a longer-term (2-hour) exposure of eggs to pyriproxyfen produced embryocidal effects. Thus, these data are collectively adequate to demonstrate the effectiveness of pyriproxyfen formulations of various dilutions against cat flea in egg, larval and adult stages when the subject product, which is a manufacturing use concentrate, is used to prepare end use products. Specific claims are dependent upon concentration, frequency of application and various other factors which are beyond the scope of this review and will need to be handled on an individual case-by-case basis. It will be necessary for either the registrant or their customers who purchase this product for use in formulating their own end use products to provide labeling outlining the types of claims which are applicable to their formulation(s).--RL Vern L. McFarland, IB"

MRID 45086801 as per an earlier review partially supports the ovicidal and larvacidal claimsmade on the proposed label of 2517-IN. The duration of claims made (9 weeks)(63 days) could not be validated from the cited study due to differences between the test protocol and desire use pattern. The registrant may include these claims, only if it is agreed that they will submit or cite confirmatory data within 12 months.

Data Submited in Support of (S)-Methoprene Activity

MRID 46041303. Miller, T. 2003. Dose Titration of an S-Methoprene Spot-On (sic) Dogs: Final Report, Statistical Analyses and Conclusions. Unpublished study prepared in cooperation with Auburn University. 19 p.

The primary objective was to determine the dose rate of s-methoprene in a spot-on formulation that would provide one month of residual flea ovisterilant activity on dogs: Regression-correlation analyses showed that only when the dose rate was logarithmically transformed ($\log_N$ mg/kg) was there a highly significant correlation between dose rate and duration of residual flea ovisterilant efficacy at the 90% level. The resultant regression equation predicted that a dose rate of 2.8 mg/kg provides 30 days of efficacy at 90%. The correlation between dose rate and residual efficacy at the 100% level was not statistically significant. However, flea eggs collected on day 31 from the two cats treated at the highest dose rates of 3.5 to 3.6 mg/kg were all sterile, indicating that the predicted dose rate for a 100% residual efficacy claim is near these values.

The data submitted are partially acceptable. The study dose rate (~3.5 mg/kg) and proposed dose rate (2.8 mg/kg) are consistent with the proposed label rate. The data do not fully support the desired label claim of 1 month flea ovisterilant; however, the claim is acceptable on the condition that the registrant agree to submit confirmatory data within 12 months.

ENTOMOLOGIST'S COMMENTS AND RECOMMENDATIONS:

The data submitted are marginally adequate to support the desired registrations. However, the registrant has agreed to submit or cite confirmatory data within 12 months to verify the conclusions drawn from an amalgamation of data on Cyphenothrin, Pyriproxyfen, and (S)-Methoprene. In the interim, the data are adequate to support the following claims:

EPA Reg. Nos. 2517-IL, 2517-IN, & 2517-ON

{[Kills][Controls][Repels]] {[Fleas][Ticks]} for up to [[28 days][4 weeks][1 month]]

EPA Reg. No. 2517-IN

Kills [flea eggs][flea larvae] for up to [63 days][9 weeks].

EPA Reg. No. 2517-ON

Kills [flea eggs] for up to [24 days][4 weeks][1 month].

Additional comments are provided on the individual labels attached.

Enclosure
002517-000IN,-ON 2006NOV7
2517-IL label
2517-IN label
2517-ON label

FEE

DATE OUT: 03/FEB/2005

FEE: PRODUCT CHEMISTRY REVIEW OF: Manufacturing-Use [ ] End-Use Product [X]
DP BARCODE:D305947 EPA RECEIVED DATE:27/JUL/2004 FILE SYMBOL/REG:2517-IN
PRODUCT:Sergeant's Cyphenothrin+IGR Squeeze-On For Dogs MRID 461661-01 & -02 ACTION R31
COMPANY : Sergeant's Pet Care Products, Inc. NON-FOOD USES [X] DECISION NO.: 338118
PPC NUMBER OF THE TGAIsIN THE PRODUCT: 129013, 129032

FROM: Sami Malak, Chemist
Technical Review Branch/RD (7505C)

TO: 13 George LaRocca/Linda DeLuise
Insecticide Branch/RD (7505C)

INTRODUCTION:

In a letter dated 15/JUN/2004, Brazos Associates, Inc. an agent for the applicant requested registration of subject product. In support of this action, the applicam included product chemistry data, a proposed label, a proposed basic CSF dated 29/DEC/2003, Formulator's Exemption, Certificate with respect to Citation of Data, and data Matrix..

FINDINGS:

1a. The subject product was produced by a non-integrated formulation system, meaning that the two active ingredients in the product are registered. The product contains 40% Cyphenothrin, Reg. No. [redacted] plus 2% Nylar, Reg. No. [redacted]

1b. The subject product, an insecticide, is intended for insect comrol infesting dogs and puppies older than 12 weeks.

2a. The applicant should be advised to submit product chemistry data requirements pertaining to the storage stability (GRN 830.6317) and corrosion characteristics (GRN 830.6320) identified in this memorandum as data gaps.

2b. Except for the data gaps in Finding 2(a) above, the submitted/referenced product chemistry data is adequate and support registration of subject product.

3. Adequate analytical method is available for enforcement. The method was previously submitted and reviewed in connection with registration of the technical sourcess, Cyphenothrin, Reg. No. [redacted] and Nylar, reg. No. [redacted]

4. The label claim nominal concentrations of 40% Cyphenothrin plus 2% Nylar are consistent with that in the submitted basic CSF dated 16/JUN/2004, both are in compliance with the regulations of PR Notice 91-2. Further, the storage and disposal statement and the physical or chemical hazards statement are in compliance with the regulations of 40CFR§156.78.

5. The proposed basic CSF dated 29/DEC/2003, was filled out correctly in compliance with the regulations of PR Notice 91-2. Further, the upper and lower certified limits are within the standard limits of 40CFR§158.175(b)(2). All ingredients claimed in the CSF are cleared for use in pesticide formulations intended for non-food uses.

CONCLUSIONS: After resolving Finding 2(a) above, the TRB will have no objections for registration of subject product.

REVIEW OF PRODUCT CHEMISTRY DATA:

1. A statement of data confidentiality dated 29/DEC/2003 was included with this submission claiming confidentiality of some of the submitted data on the basis of its falling within the scope of FIFRA§10(d)(1)(A), (B), or (C). Review of CBI data has been removed to Confidential Appendix A.

2. A GLP statement dated 20/MAR/2003 was included with this submission to the effect that some of the submitted studies were conducted in compliance with the GLP requirements of 40CFR§160.

DATA SUBMITTED

Group A, Series 830-Product Identity, Composition, and Analysis (40 CFR 155, 160, 162, 167, 175 & 180)

830-1550 Product Identity and Composition

This product contains two registered technical grade of an active ingredients plus cleared inert ingredients intended for non-food uses (refer to product's basic CSF dated 29/DEC/2003).

830-1600 Description of Materials Used to Produce the Product:
Refer to Confidential appendix A.

830-1650 Description of Formulation Process:
Refer to Confidential appendix A.

830-1670 Discussion of Formation of Impurities:
Refer to Confidential appendix A.

830-1700 Preliminary Analysis:
Refer to Confidential appendix A.

830-1750 Certified Limits:
Refer to Confidential appendix A.

830-1800 Enforcement Analytical Method:

Adequate analytical method is available for enforcement. The method was previously submitted and reviewed in connection with registration of the technical sourcess, Cyphenothrin, Reg. No. [redacted] and Nylar, reg. No. [redacted]

Identity, Composition, Formulation, and Analysis, Subgroup A, Series 830.1550 to 830.1800 (40 CFR 158.155 to 158.180)

Guideline Reference NO.(GRN 830.)/Title	Data Fulfilled	MRID No.
.1550 Product identity and composition	Y	461661-01
.1600 Description of materials used to produce the product	Y	461661-01
.1650 Description of formulation process	Y	461661-01
.1670 Discussion of formation of impurities	Y	461661-01
.1700 Preliminary analysis	Y	461661-01
.1750 Certified limits	Y	461661-01
.1800 Enforcement analytical method	Y	461661-01

Physical and Chemical Properties, Subgroup B, Series 830.6302 to -830.7300 (40 CFR 158.190)

Guideline Reference NO.(GRN 830.)/Title	Data Fulfilled	Value or Qualitative Description	MRID No.
.6302 Color	Y	Yellow.	461661-02
.6303 Physical state	Y	Liquid.	461661-02
.6304 Odor	Y	Odorless.	461661-02
.6314 Oxidation/seduction: Chemical incompatibility	NA	Does not contain an oxidising or reducing agents.	
.6315 Flammability/flame extension	Y	>200°F.	461661-02
.6316 Explodability	NA	Not considered to be explosive.	
.6317 Storage stability	G		
.6319 Miscibility	Y	Completely miscible in aromatics, petroleum distillates and alcohols. Immiscible in water.	461661-02
.6320 Corrosion characteristics	G	..	
.6321 Dielectric breakdown voltage	NA	It is not recommended for use around electrical equipment.	
.7000 pH	NA	Insoluble in water.	
.7100 Viscosity	Y	94.5 cps @ 23°C.	461661-02
.7300 Density/relative density/bulk density	Y	1.079 @ 24°C.	461661-02

Explanations: Y =The requirements were fulfilled; N = The requirements not fulfilled; N/A = Not applicable; G = Data gap; U = Requires upgrading; I = Incomplete or in progress; W = Waived.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: October 12, 2005

MEMORANDUM

Subject: EPA File Symbol: 2517-IN SERGEANT'S CYPHENOTHRIN + IGR SQUEEZE-ON FOR DOGS
DP Barcode: D321227
Decision No.: 338118
PC Codes: 129013 Cyphenothrin (CAS #39515-40-7), 129032 Pyriproxyfen (CAS #95737-68-1)

From: Byron T. Backus, Ph.D.
Technical Review Branch
Registration Division (7505C)

Byron T. Backus 10-12-2005

To: George LaRocca RM 13
Insecticide Branch
Registration Division (7505C)

Applicant: SERGEANT'S PET CARE PRODUCTS, INC.

FORMULATION DECLARATION FROM LABEL:

Active Ingredient(s):	% by wt
Cyphenothrin (CAS #39515-40-7)	40.0%
Nylar (CAS #95737-68-1)	2.0%
Inert Ingredients:	58.0%
Total:	100.00%

ACTION REQUESTED:

The Risk Manager requests:

"...The registrant is providing additional data we discussed at the 7/13/05 meeting."

"...You completed review of the companion animal safety study for 2517-IN, IL on Nov. 30th and Nov. 24th, 2004. Mark Suarez completed review of efficacy data (MRID 46166109) associated with these two products and noted symptoms reported in all dogs in Test Group 2 (see attached excerpt). This appears to be inconsistent with what you reported. Mark has electronically sent you a copy of the efficacy study for further consideration."

BACKGROUND:

There have been two previous TRB toxicity reviews for this product. The first (November 24, 2004) consisted of a review of 5 acute toxicity studies (the inhalation study requirement was waived) and a companion animal (including both adult dogs and 12-week-old puppies) safety study (MRID 46166108). All studies were classified as acceptable. In the companion animal safety study the only possible systemic effects that were observed following exposure to the test material at 5X were ocular discharge and salivation. No effects were noted at 1X (3X was not tested).

Subsequently (memorandum dated June 27, 2005), TRB reviewed findings from an efficacy study (MRID 46166109) in which all 6 dogs treated at what was supposedly a 1X dose showed symptoms which included head shaking and/or slight body tremors. A listing of the symptoms in individual dogs is given below:

Dog Number	Sex [(S)=Spayed]	Symptoms[a]
HHCAVJ	F(S)	Head shaking on Day 3; Slight body tremors on Day 3.
35022	M	Vomiting (Day 1); Head shaking (Days 2, 3 & 5); Licking of paws (Days 2-6); Rubbing of head and body (Day 3); Slight tremors all over body on Day 5.
CNJAZF	F(S)	Slight tremors on Day 1; Shaking on Days 1-5; Squinting on Day 1; Licking of Paws Days 3-5; Unsteadiness Day 1, Circling on Day 2; Pacing on Day 4; Rubbing of head on Day 1.
36737	F	Ear twitching Days 1-3; Head shaking on Days 1 & 3; Licking of paws on Days 1 & 5; Pacing on Days 4 & 5; Slight body tremors Days 2 & 3.
28625	F(S)	Head shaking Days 1-3, 5, 7 & 8; Ear twitching on Day 3, Licking of the paws and genitalia Days 3-4; Hair loss and irritated skin on the right shoulder onto the mid-back on Days 22-47.
34911	M	Vomiting on Day 1; Head shaking Days 1-4, 7-8; Licking of genitalia and/or paws Days 1-7; Hair loss/redness at ear tips on Days 2-5 and 7-33.

[a]Symptoms are reported (in text) on p. 19 of MRID 46166109.

There was a meeting with the registrant on 7/13/05, and the registrant has provided (letter dated July 29, 2005) additional information relating to these findings, including the following:

"...The last efficacy study (MRID 46166109) did include observations of effects at a 100 mg/kg (1X) application rate. The reported effects included effects that can be considered normal dog behavior, accentuated under laboratory confinement conditions (i.e., licking of paws and genitalia, pacing, head shaking). Additionally, vomiting is also not uncommon in dogs, under laboratory conditions. Tremors were also observed in this study. The tremors could be based on neurologic pathophysiology or they could be the result of just shaking to relieve itch or an unusual skin sensation. This study was not set up to determine the reason of such effects on the animals tested; however, it did report them in detail. We also believe that some of the reporting may be accentuated by the individual observer and that some of the effects may not have been reported at another laboratory that might consider such activities as normal animal behavior.

"Based on Sergeant's review of the Companion Animal Safety Study and the various application groups...Sergeant's would like to set a minimum weight of five pounds for dogs being treated with Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs. This will ensure that the application rate is within reason of the recommended application rate of 100 mg/kg. It will also allow Sergeant's to develop a product especially for dogs under five pounds..."

The material received also includes the following: "Cyphenothrin, like other later generation synthetic pyrethroids...are strongly contraindicated on cats because of the cat's exquisitely sensitive dermal sensory system that leads to self grooming and ingestion of the product with an often fatal outcome. The behavior of the dogs in this study are reminiscent of this phenomenon observed in cats, although much less severe than in cats. It is probably that the observed effects in the this study were caused by transient cutaneous nerve stimulation in the treated dogs and their ability (as confined, bored animals without other distractions) to apply their full-undivided attention to this issue..."

COMMENTS AND RECOMMENDATIONS:

1. The most likely explanation for the symptoms (including tremors) observed in the efficacy study was that the dogs ingested some of the test material after application.

2. Current directions for the application of this product specify to apply as a stripe from the back of the neck to base of the tail. If labeling is revised to specify application of the product from the back of the neck to a point midway between the neck and tail then the dog would not be able to reach any part of the application site and so would be unable to ingest the product by licking. With this labeling revision, TRB would have no objections to the registration of the proposed product.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: June 27, 2005

MEMORANDUM

Subject: EPA File Symbol: 2517-IN SERGEANT'S CYPHENOTHRIN + IGR SQUEEZE-ON FOR DOGS
DP Barcode: D317320
Decision No.: 338118
PC Codes: 129013 Cyphenothrin (CAS #39515-40-7), 129032 Pyriproxyfen (CAS #95737-68-1)

From: Byron T. Backus, Ph.D.
Technical Review Branch
Registration Division (7505C)

Byron T. Backus 6-27-05 VCR

To: George LaRocca RM 13
Insecticide Branch
Registration Division (7505C)

Applicant: SERGEANT'S PET CARE PRODUCTS, INC.

FORMULATION DECLARATION FROM LABEL:

Active Ingredient(s):	% by wt
Cyphenothrin (CAS #39515-40-7)	40.0%
Nylar (CAS #95737-68-1)	2.0%
Inert Ingredients:	58.0%
Total:	100.00%

ACTION REQUESTED:

The Risk Manager requests:

"...You completed review of the companion animal safety study for 2517-IN, IL on Nov. 30th and Nov. 24th, 2004. Mark Suarez completed review of efficacy data (MRID 46166109) associated with these two products and noted symptoms reported in all dogs in Test Group 2 (see attached excerpt). This appears to be inconsistent with what you reported. Mark has electronically sent you a copy of the efficacy study for further consideration."

BACKGROUND:

This review compares the findings in the previously reviewed companion animal safety study (MRID 46166108) with those of the efficacy data (MRID 46166109) on this proposed product.

COMMENTS AND RECOMMENDATIONS:

1. In the companion animal safety study (MRID 46166108) no symptoms were observed in the 1X dogs; at the 5X dose level possible systemic effects included ocular discharge and salivation, and there was a slight mean weight decrease in this group in the period from Day -3 to Day 7. However, there were no indications of neurological symptoms (including tremors, shaking, head shaking) in the 5X group. In contrast, in the efficacy study (MRID 46166109), all 6 dogs treated at what was supposedly a 1X dose showed symptoms (including those of a neurological nature), as indicated below:

Dog Number	Sex [(S)=Spayed]	Symptoms[a]
HHCAVJ	F(S)	Head shaking on Day 3; Slight body tremors on Day 3.
35022	M	Vomiting (Day 1); Head shaking (Days 2, 3 & 5); Licking of paws (Days 2-6); Rubbing of head and body (Day 3); Slight tremors all over body on Day 5.
CNJAZF	F(S)	Slight tremors on Day 1; Shaking on Days 1-5; Squinting on Day 1; Licking of Paws Days 3-5; Unsteadiness Day 1, Circling on Day 2; Pacing on Day 4; Rubbing of head on Day 1.
36737	F	Ear twitching Days 1-3; Head shaking on Days 1 & 3; Licking of paws on Days 1 & 5; Pacing on Days 4 & 5; Slight body tremors Days 2 & 3.
28625	F(S)	Head shaking Days 1-3, 5, 7 & 8; Ear twitching on Day 3, Licking of the paws and genitalia Days 3-4; Hair loss and irritated skin on the right shoulder onto the mid-back on Days 22-47.
34911	M	Vomiting on Day 1; Head shaking Days 1-4, 7-8; Licking of genitalia and/or paws Days 1-7; Hair loss/redness at ear tips on Days 2-5 and 7-33.

[a]Symptoms are reported (in text) on p. 19 of MRID 46166109.

2. In the companion animal safety study (MRID 46166108) at 1X dogs weighing <6.6 kg (all puppies) were treated with 1.17 mL (the amount of material that could be applied from a 1.5 mL ampule) test material; those weighing from 6.8-15 kg were also treated with 1.17 mL; those weighing 15.1-29.5 kg were treated with 2.34 mL (2 x 1.17 mL),

while those weighing >29.5 kg were treated with 3.51 mL (3 x 1.17 mL). At the 5X dose level puppies weighing <6.6 kg were treated with 5.85 mL (5 x 1.17 mL); dogs weighing 6.8-15 kg were also treated with 5.85 mL; dogs weighing 15.1-29.5 kg were treated with 11.7 mL (10 x 1.17 mL) and dogs weighing >29.5 were treated with 17.55 mL (15 x 1.17 mL).

From p. 18 of MRID 46166109: "Two male and four female (three of which were spayed) dogs were allocated to Test Group 2. All dogs had short hair..." The following are the body weights of these dogs and the amount of test material applied:

Dog Number	Sex [(S) = Spayed]	Weight (kg)	Dose (mL)[a]	1X Label Dose (mL)
HHCAVJ	F(S)	10.9	2.5	1.17
35022	M	7.7	1.7	1.17
CNJAZF	F(S)	9.2	2.1	1.17
36737	F	6.8	1.5	1.17
28625	F(S)	12.2	2.8	1.17
34911	M	13.6	3.1	1.17

[a]Individual dosages in the efficacy study are presented on p. 31 of MRID 46166109.

In the efficacy study (MRID 46166109) dogs were then treated with from 1.45X to 2.65X the indicated label dosage rate (the mean dose of 2.3 mL was 1.97X the indicated label dosage rate; according to information on p. 84 of MRID 46166109 the dosage rate in the efficacy study was 100 mg cyphenothrin/kg b.w.). The 5X dogs in the companion animal safety study weighing 6.8 - 15 kg were treated with 5.85 mL, or about 2.54X the dose that animals received in the efficacy study.

3. There are obviously then some significant inconsistencies between the findings of the companion animal safety study in MRID 46166108 and the efficacy study in MRID 46166109. The occurrence of neurological signs of toxicity in all 6 dogs in the efficacy study suggests that there is not even a 2X margin of safety associated with the proposed application rate of 1.17 mL in at least some dogs weighing from 6.8 - 15 kg, while the efficacy study data, as submitted, were conducted using a dose rate higher than that of the previously reviewed proposed label.

4. The registrant should be informed of these inconsistencies. The proposed product should not be registered until the issues (margin of safety involved in the use of this product, whether the efficacy data, using a higher dose application rate than that of the proposed label, can be used to support this registration) raised by these inconsistencies have been adequately addressed.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: November 24, 2004

MEMORANDUM

40

Subject: EPA File Symbol: 2517-IN SERGEANT'S CYPHENOTHRIN + IGR SQUEEZE-ON FOR DOGS
DP Barcode: D305948
Decision No.: 338118
PC Codes: 129013 Cyphenothrin (CAS #39515-40-7), 129032 Pyriproxyfen (CAS #95737-68-1)

From: Byron T. Backus, Ph.D.
Technical Review Branch
Registration Division (7505C)

Byron T. Backus 11-24-2004 JCR

To: Linda DeLuise/George LaRocca RM 13
Insecticide Branch
Registration Division (7505C)

Applicant: SERGEANT'S PET CARE PRODUCTS, INC.

FORMULATION DECLARATION FROM LABEL:

Active Ingredient(s):	% by wt
Cyphenothrin (CAS #39515-40-7)	40.0%
Nylar (CAS #95737-68-1)	2.0%
Inert Ingredients:	58.0%
Total:	100.00%

ACTION REQUESTED:

The Risk Manager requests:

> Tox waiver request for acute inhalation; review of 5 other acute studies and a companion animal study.

BACKGROUND:

This package includes an acute oral LD_{50} study (rat, up-and-down procedure, defaulting to an acute toxic class procedure, MRID 46166103); acute dermal LD_{50} study (rat; MRID 46166104); primary eye irritation study (rabbit; MRID 46166105); primary dermal irritation study (rabbit; 46166106) and a dermal sensitization study (guinea pig; 46166107), as well as a companion animal safety study in dogs (MRID 46166108). The five acute toxicity studies were conducted at Product Safety Labs, New Jersey. The companion animal safety study was conducted at Stillmeadow, Inc. In addition, there is a waiver request for an inhalation study. All studies were conducted on Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL, containing 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar.

RECOMMENDATIONS:

1. The companion animal (dog) safety study in MRID 46166108 has been reviewed and has been classified as acceptable for puppies (12 weeks and older) and adult dogs. It is concluded that there is an adequate margin of safety (at least 5X) between the exposure associated with the proposed use level for this formulation in dogs, and that at which significant adverse systemic effects (not seen in this study, but which might include ear twitching, muscle tremors, drooling) may occur. For dermal effects an effect was observed in one puppy in Group III (treated at essentially a 7.5X dose level), but in none of the other dogs (including the puppies in Group II, dosed at 1.5X) indicating a reasonably low potential for this effect in dogs treated at the proposed use level.

2. It is noted that the test material was supplied in (and applied from) unidose 1.5 mL ampules. However, the report states that the mean volume delivered from a single 1.5 mL ampule was 1.17 mL, and the registrant is proposing packaging this product in 3.0 and 4.5 (as well as 1.0 and 1.5) mL tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2 x 1.17) mL and the 4.5 mL tubes deliver no more than 3.51 (3 x 1.17) mL.

3. The five acute toxicity studies have been reviewed and classified as acceptable. In addition, TRB has no objection to the registrant's waiver request for an acute inhalation study, based on the product form (a yellow liquid), its proposed packaging

(1.0, 1.5, 3.0 or 4.5 mL tubes or ampules), the method of application (as a spot-on or stripe-on to the dog's back), and the relatively low inhalation toxicity of technical Cyphenothrin (one report from the open literature gives a rat LC50 of 1.85 mg/L, or EPA toxicity category III; extrapolating from this the inhalation LC50 value for a 40% Cyphenothrin-60% inert product would then be greater than 4 mg/L, or EPA toxicity category IV by this exposure route).

4. Based on the results of the acute toxicity studies, the following is the acute toxicity profile for EPA File Symbol: 2517-IN SERGEANT'S CYPHENOTHRIN + IGR SQUEEZE-ON FOR DOGS. The signal word of the product would be CAUTION, as proposed by the registrant:

Study Type	Tox. Cat.	Classification & MRID #
Acute Oral LD_{50} (rat)	III	Acceptable (#46166103)
Acute Dermal LD_{50} (rat)	III	Acceptable (#46166104)
Acute Inhalation LC_{50}	IV	Waived
Primary Eye Irritation (rabbit)	III	Acceptable (#46166105)
Primary Dermal Irritation (rabbit)	IV	Acceptable (#46166106)
Dermal Sensitization (guinea pig)	Negative	Acceptable (#46166107)

5. Based on the acute toxicity profile and proposed uses, the following is the precautionary labeling for this product, as obtained from the Label Review System:

PRODUCT ID #: **002517-00080**

PRODUCT NAME: **SERGEANT'S CYPHENOTHRIN + IGR SQUEEZE-ON FOR DOGS**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **CAUTION**

Hazards to Humans and Domestic Animals:

Harmful if swallowed or absorbed through skin.. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical advice.

Reviewer: Byron T. Backus, Ph.D. Date: November 19, 2004
Risk Manager (EPA): 13

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 46661 03) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs (although this product does not contain Methoprene) with a label declaration of: Cyphenothrin 40.0% and Pyriproxyfen (Nylar) 2.0%.

CITATION: Moore, G. (2003) Acute Oral Toxicity Up and Down Procedure in Rats: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13320, P320/UDP. Unpublished study prepared by Product Safety Labs, Food Product Laboratory and Silliker Laboratories of New Jersey, Inc. 16 p. Study Completion Date: May 20, 2003. MRID 46166103.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46166103), conducted using the up-and-down procedure but defaulting to the acute toxic class method, Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Gokilaht (Cyphenothrin), 3.0% Methoprene and 2.00% Nylar was administered by oral gavage at 2000 mg/kg to a single Sprague-Dawley derived 9-week-old albino fasted (overnight) female rat. When this rat survived, four additional fasted (overnight) female rats of the same strain, age, body weight range (164-182 g) and source (Ace Animals, Inc., Boyertown, PA) were also dosed at 2000 mg/kg.

On the day of dosage rats were observed for several hours for mortality and signs of gross toxicity for several hours post-dosing. They were then observed at least once a day for the remainder of the 14-day observation period.

On the day of dosage rats were observed at least 3 times within the first 4 hours after dosing for clinical signs of toxicity and mortality and then at least once daily for the remainder of the 14-day observation period. Individual body weights were recorded just prior to dosing (Day 0) and on days 7 and 14. Individual body weights were recorded predosing and on days 7 and 14.

Two rats died within 24 hours of dosage with no clinical signs observed prior to death. Two rats which survived showed reduced fecal volume, ventral staining and hypoactivity, with recovery by Day 4. All survivors gained weight in the period from Day 0 (predose) to Day 7 and again from Day 7 to 14.

Postmortem necropsy findings in the rats which died showed discoloration of the lungs and intestines and fluid filled stomachs. Gross necropsy findings in rats surviving to terminal sacrifice were unremarkable.

Estimated Oral LD_{50} in female rats > 2000 mg/kg.

EPA File Symbol 2517-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.06 t g/mL containing 40% Cyphenothrin and 2% Pyriproxyfen (Nylar) is in EPA toxicity category III in terms of oral exposure based on the observed LD_{50} (>2000 mg/kg) in female rats.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870. t t00; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 16), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Friday, October t5, 2004, 4:37:t t PM
Data file name: Cyphenothrin-IGR.dat
Last modified: 10/t5/2004 4:37:11 PM

Test/Substance: Cyphenothrin-IGR
Test type: Limit Test
Limit dose (mg/kg): 2000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
t	8040	2000	O	O
2	8t98	2000	O	O
3	8239	2000	O	O
4	8372	2000	X	X
5	9407	2000	X	X

(X = Died, O = Survived)

Dose Recommendation: The limit test is complete.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
2000	3	2	5
All Doses	3	2	5

Statistical Estimates:

The LD50 is greater than 2000 mg/kg.

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	-	2/5	-

Statistics - Not necessary to compute the oral LD_{50}.

A. **Mortality** - As noted in the table above.

B. **Clinical observations** - Two rats died within 24 hours of dosage with no clinical signs observed prior to death. Two rats which survived showed reduced fecal volume, ventral staining and hypoactivity, with recovery by Day 4. All survivors gained weight in the period from Day 0 (predose) to Day 7 and again from Day 7 to 14.

C. **Gross Necropsy** - Postmortem necropsy findings in the rats which died showed discoloration of the lungs and intestines and fluid filled stomachs. Gross necropsy findings in rats surviving to terminal sacrifice were unremarkable.

D. **Reviewer's Conclusions:** The study is acceptable. EPA File Symbol 2517-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 40% Cyphenothrin and 2% Pyriproxyfen (Nylar) is in EPA toxicity category III in terms of oral toxicity based on the observed LD_{50} (>2000 mg/kg) in female rats.

E. **Deficiencies** - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 22, 2004
Risk Manager (EPA): 13

STUDY TYPE: Acute Dermal Toxicity - Wistar rats - OPPTS 870.1200; OECD 402

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs (although this product does not contain Methoprene) with a label declaration of: Cyphenothrin 40.0% and Pyriproxyfen (Nylar) 2.0%.

CITATION: Moore, G. (2003) Acute Dermal Toxicity Study in Rats - Limit Test: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13321, P322. Unpublished study prepared by Product Safety Labs, Food Product Laboratory and Silliker Laboratories of New Jersey, Inc. 16 p. Study Completion Date: May 20, 2003. MRID 46166104.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID #46166104), a group (5M & 5F) of Sprague-Dawley derived albino rats (source: Ace Animals, Inc., Boyertown, PA; Males: 300-318 g; Females: 178-204 g; young adult [indicated by body weight data]) were dermally exposed (approximately 10% of body surface) for 24 hrs to 2000 mg/kg of undiluted Cyphenothrin-IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen). The test material was held in contact by a gauze pad and Durapore tape.

Rats were observed several times after application on day 0 and once daily thereafter for 14 days. Individual body weights were recorded just prior to dosing (day 0) and on days 7 and 14.

There was no mortality and there were no signs of systemic toxicity. Three males showed some dermal irritation (erythema and/or edema) with clearing by day 2. All rats gained weight from day 0 to 7 and from day 7 to 14.

No gross abnormalities were observed at post-sacrifice necropsy.

Dermal LD_{50} Males > 2000 mg/kg (0/5 died)
Females > 2000 mg/kg (0/5 died)
Combined > 2000 mg/kg (0/10 died)

Based on the rat LD_{50} > 2000 mg/kg, Cyphenothrin-IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar is in EPA toxicity category III in terms of dermal toxicity.

This acute dermal study is classified as acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 16), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Statistics - Not necessary to compute the dermal LD_{50}.

A. Mortality - None, as noted in the table above.

B. Clinical observations - There were no signs of systemic toxicity. Three males showed some dermal irritation (erythema and/or edema) with clearing by day 2. All rats gained weight from day 0 to 7 and from day 7 to 14.

C. Gross Necropsy - No gross abnormalities were observed at post-sacrifice necropsy.

D. Reviewer's Conclusions: The study is acceptable. Based on the rat LD_{50} > 2000 mg/kg, Cyphenothrin-IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is in EPA toxicity category III in terms of dermal toxicity.

E. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 23, 2004
Risk Manager (EPA): 13

STUDY TYPE: Primary Eye Irritation - NZW Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs (although this product does not contain Methoprene) with a label declaration of Cyphenothrin 40.0% and Pyriproxyfen (Nylar) 2.0%.

CITATION: Moore, G. (2003) Primary Eye Irritation Study in Rabbits: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13322, P324. Unpublished study prepared by Product Safety Labs, Food Products Laboratory and Silliker Laboratories of New Jersey, Inc. 17 p. Study Completion Date: May 20, 2003. MRID 46166105.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46166105), 0.1 mL of undiluted Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen), was instilled into the conjunctival sac of one eye of each of 3 adult New Zealand White Rabbits (weights: not reported; ages: young adult; source: Davidson's Mill Farm, South Brunswick, NJ), with observations and scoring at 1, 24, 48 and 72 hours after instillation.

No corneal opacity was observed (with 2% ophthalmic fluorescein sodium used at 24 hours to verify the absence of corneal opacity at that reading). 3/3 eyes were positive for conjunctival redness (score of 2) at 1 and 24 hours. All eyes were completely clear (all scores zero) at 72 hours.

In this study, Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is in EPA toxicity category III based on the presence of grade 2 conjunctival redness in 3/3 eyes at 24 hrs which subsequently cleared by 72 hrs.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 17), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested			
	1 hr	24 hrs[2]	48 hrs	72 hrs
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness[1]	3/3	3/3	0/3	0/3
Chemosis[1]	0/3	0/3	0/3	0/3
Discharge[1]	3/3	0/3	0/3	0/3

[1]Score of 2 or more considered positive
[2]Fluorescein staining was used to verify the absence of corneal opacity.

A. **Observations** - No systemic effects were observed. 3/3 eyes were positive for conjunctival redness (score of 2) at 1 and 24 hours. All eyes were completely clear (all scores zero) at 72 hours.

B. **Reviewer's Conclusions:** The study adequately defines a Toxicity Category III hazard potential in terms of eye exposure potential for Cyphenothrin-IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen).

C. **Deficiencies** - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 23, 2004
Risk Manager (EPA): t3

STUDY TYPE: Primary Dermal Irritation - NZW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. t1 of MRID 46 t66 t04 the specific gravity of the test material was 1.06 t g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 25 t7-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs (although this product does not contain Methoprene) with a label declaration of Cyphenothrin 40.0% and Pyriproxyfen (Nylar) 2.0%.

CITATION: Moore, G. (2003) Primary Skin Irritation Study in Rabbits: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13323, P326. Unpublished study prepared by Product Safety Labs, Food Products Laboratory and Silliker Laboratories of New Jersey, Inc. t7 p. Study Completion Date: May 20, 2003. MRID 46166106.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46166 t06), 0.5 mL aliquots of undiluted Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of t.06 t g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen), were applied to dermal sites on each of 3 (2M & 1F) young adult New Zealand White albino rabbits (source: Davidson's Mill Farm, South Brunswick, NJ) with 4-hour semioccluded exposure.

After 4 hours, the gauze patch and holding tape were removed. The test sites were scored (Draize) at t, 24, 48 and 72 hrs and at 7 and 10 days.

No edema was observed (all scores for edema were zero). All sites scored one for erythema at 1 hour and 2 at 24, 48 and 72 hours. One site scored 2 for erythema on day 7 while the other two scored 1. All scores were zero on day t0. The PII (average of scores at 1, 24, 48 & 72 hrs) = 1.75.

In this study, Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of t.06 t g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is in EPA Toxicity Category IV for dermal irritation effects, based on the PII of 1.75 and relatively low score (grade 2, characterized as well-defined) for erythema at 72 hrs [EPA Toxicity Category III would be characterized by moderate or grade 3 erythema at 72 hrs) following 4-hr semi-occluded exposure.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 17), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

A. Observations - No edema was observed (all scores for edema were zero). All sites scored one for erythema at 1 hour and 2 at 24, 48 and 72 hours. One site scored 2 for erythema on day 7 while the other two scored 1. All scores were zero on day 10. The PII (average of scores at 1, 24, 48 & 72 hrs) = 1.75.

B. Results - The PII (average of 1, 24, 48 and 72-hour scores) = 1.75 The mean irritation score on day 3 was 2.0 (erythema: 2.0; edema: 0.0).

C. Reviewer's Conclusions - The study adequately demonstrates a Toxicity Category IV hazard potential in terms of dermal irritation for Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen).

D. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 23, 2004
Product Manager (EPA): 13

STUDY TYPE: Dermal Sensitization - albino Guinea Pig; OPPTS 870.2600; OECD 406, 429

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IN Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs (although this product does not contain Methoprene) with a label declaration of Cyphenothrin 40.0% and Pyriproxyfen (Nylar) 2.0%.

CITATION: Moore, G. (2003) Dermal Sensitization Study in Guinea Pigs: Buehler Method: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13324, P328. Unpublished study prepared by Product Safety Labs, Food Products Laboratory and Silliker Laboratories of New Jersey, Inc. 25 p. Study Completion Date: May 20, 2003. MRID 46166107.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46166107) with Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen), a group of 20M Hartley albino guinea pigs (373-428 g; young adult; source: Elm Hill Breeding Labs, Chelmsford, MA) were each dermally exposed (6 hours) to a 0.4 mL aliquot of test material on a once-a-week basis for 3 consecutive weeks. After a two week rest period they were then dermally challenged with 0.4 mL of a 75% w/w mixture of the test material in mineral oil at a previously unexposed site. An additional 10 previously unexposed male guinea pigs received were similarly treated. Challenge sites on all 30 guinea pigs were evaluated and scored for erythema at 24 and 48 hours after the application.

Following challenge, 7/20 previously exposed guinea pigs showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours. 4/10 controls showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours.

The report includes results from a positive control study (PSL Study #12371) which was conducted with technical (85%) alpha-Hexylcinnamaldehyde and completed on August 15, 2002. The results (3/10 previously exposed, 0/5 naive control guinea pigs showing a positive response at challenge) were appropriate. The study dates for the testing with Cyphenothrin-IGR Squeeze-On for Dogs were from March 13 to April 11, 2003. While slightly outside the 6-month period indicated in the Guidelines, it is concluded the overall study findings are acceptable.

In this study there were no indications that Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is a dermal sensitizer.

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406, 429) in the Guinea pig.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 25), and [No] Data Confidentiality (p. 2) statements were provided.

I. PROCEDURE

A. Induction - Each of 20 male Hartley albino guinea pigs was treated once a week for 3 consecutive weeks to a 6-hour exposure to 0.4 mL undiluted Cyphenothrin-IGR Squeeze-On for Dogs.

B. Challenge - Twenty-seven days after the first induction exposure 0.4 mL of a 75% w/w mixture of the test material in mineral oil was applied to a naive site on the right side of each guinea pig at a previously unexposed site. These sites were evaluated and scored for erythema at 24 and 48 hours after the challenge application.

C. Naive Controls - At the time the 20 previously induced guinea pigs were challenged, 10 previously unexposed (negative control) guinea pigs were similarly challenged.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Following challenge, 7/20 previously exposed guinea pigs showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours. 4/10 controls showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours.

B. Positive control - The report includes results from a positive control study (PSL Study #12371) which was conducted with technical (85%) alpha-Hexylcinnamaldehyde and completed on August 15, 2002. The results (3/10 previously exposed, 0/5 naive control guinea pigs showing a positive response at challenge) were appropriate. The study dates for the testing with Cyphenothrin-IGR Squeeze-On for Dogs were from March 13 to April 11, 2003. While slightly outside the 6-month period indicated in the Guidelines, it is concluded the overall study findings are acceptable.

C. Reviewer's Conclusions: **Based on the results of this study Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is not a dermal sensitizer.**

D. Deficiencies - The final date for the cited positive control study is approximately 7 months before the initiation of this study. However, TRB can accept the results of this study.

EPA Primary Reviewer: Byron T. Backus, Ph.D. Signature: Byron T. Backus
Technical Review Branch, Registration Division (7505C) Date 11/15/2004
EPA Secondary Reviewer: William Dykstra, Ph.D. Signature: William Dykstra
Health Effects Division (7509C) Date 11/17/04

DATA EVALUATION RECORD

STUDY TYPE: Companion Animal Safety - Dogs OPPTS 870.7200

PC CODES: 129013 (Cyphenothrin), 129032 DP BARCODE: D305948
RISK MANAGER: (EPA): 13 DECISION NO.:338118

PRODUCT AND TEST MATERIAL: Cyphenothrin-IGR Spot-on for Dogs. [EPA File Symbol 2517-IN], a liquid labeled "Gokilaht Spot-On w/IGR's (2824) 40.00% RS-Gokilaht; 3.00% S-Methoprene; 2.00% Nylar." According to a certificate of analysis (p. 47 of MRID 46166108) the formulation contained 39.87% Gokilaht, 3.00% S-Methoprene and 2.00% Nylar. Packaged in unidose ampules containing 1.5 mL product.

CITATION: Kuhn, J. (2003) Companion Animal Safety Study in Dogs: Cyphenothrin-IGR Spot-on for Dogs. Final Report. Project Number 7650/03. Unpublished study prepared by Stillmeadow, Inc. and Miller, Thomas A. 53 p. Study Completion Date: 20 October 2003. MRID 46166108.

SPONSOR: Sergeant's Pet Care Products, Inc. Omaha, NE 68130-1703.

EXECUTIVE SUMMARY: In a companion animal safety study (MRID 46166108), groups of 12 dogs (from 5 to 9 males in each group) with each group including three 12-week old puppies weighing 4.1-6.1 kg, 2 or 3 dogs weighing 6.8-15 kg, 3 or 4 dogs weighing 15.1-29.5 kg, and 3 weighing >29.5 kg) were dosed with: 1) the amount of vehicle contained in a single dose (Group I, controls); 2) at 1X the label use directions (except for puppies, which were dosed at 1.5X) in Group II, and 3) at 5X the label use directions (except for puppies, which were dosed at 7.5X) in Group III. Group III dogs were treated five times with one hour between each treatment.

The test material was supplied in unidose 1.5 mL ampules. However, the report states that the mean volume delivered from one of these ampules was 1.17 mL. One dose for puppies consisted of material from a single 1.5 mL ampule (the proposed label states that dogs weighing less than 15 lbs [= 6.8 kg] are to be treated with 1.0 mL), for dogs weighing 15-33 lbs (6.8-15 kg) it was 1.5 mL, for dogs weighing 15.1-29.5 kg it was the contents of two 1.5 mL ampules (the proposed label says two 1.5 mL or one 3.0 mL ampule), and for dogs weighing >29.5 kg it was three 1.5 mL ampules (the proposed label says three 1.5 mL or one 4.5 mL ampules). The control material was supplied in bulk and placebo controls were treated with this formulation (without actives) at the rate of 55.13% of the active product dose volumes.

Administration was according to the proposed label directions and involved application of the test substance (or control vehicle) to the skin in a line along the spine starting at the back of the neck. Label directions specify application of the product as a spot-on or stripe treatment between the shoulder blades to dogs weighing up to 15 kgs. For dogs weighing between 15 and 29.5 kg application would be as a spot-on or stripe treatment at two sites on the back, one

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between the shoulder blade and one diredly in front of the base of the tail. For >29.5 kg the contents of one 1.5 mL ampule would be applied to the back as a spot-on or stripe between the shoulder, and the contents of the other two 1.5 mL ampules would be applied as a stripe on the back in front of the base of the tail.

Each dog in Groups I and II was observed at 1, 2, 3 and 4 hours following treatment on Day 0. Group III dogs were also observed "between the hourly dosings" (1, 2, 3, 4, 5, 6, 7 and 8 hours after the first treatment). All dogs were then observed twice (a.m. and p.m.) on Days 1-15.

Individual body weights were determined on Days -7, -3, 7 and 14. Individual food consumption was determined on a daily basis from Day -7 through Day 15 by measuring the amount of food given to each dog in the morning and subtracting the amount left at the end of the day. Blood samples were taken on Days -7 and 1 following overnight fasts.

Possible systemic effects related to exposure to the test material included ocular discharge and salivation. In the immediate period following treatment, ocular discharge was observed in one Group II dog (a puppy) at 4 hours post-dose, and in 4 Group III dogs (including all three puppies). Salivation (mostly very slight, but in some cases moderate) was observed in five Group III dogs (including 1/3 puppies), and was observed (very slight) in one adult 32.2 kg dog at 1 hour postdose (so at this time this dog had presumably been treated with only 1 or 2 applications of test material). Salivation was seen in another Group III adult starting at 3 hours, and in two additional Group III adults starting at 4 hours. During the subsequent 15-day observation period, ocular discharge was frequently observed (including continuously from day 10 to 15) in one control puppy, in none of the Group II (1X) dogs, and in one Group III puppy (days 1-2) and one Group III adult (days 1-6, then again on Days 13-15); both of these Group III animals had also shown ocular discharge in the period immediately following the first treatment. Salivation was observed in one Group III adult male at the AM observation on Day 1 (this dog had also showed salivation during the 8-hour period following the first treatment). One Group III male puppy showed a lesion (or lesions) on both sides of the shoulder (presumably at or near the application site) from Day 5 through 15, and was observed to scratch this area frequently.

Group III adults showed a mean weight loss between days -3 and +7. The incidences of adult dogs showing weight losses between days -3 and +7 were: Group I: 3/9; Group II: 4/9; Group III: 6/9. It is concluded then that for adult dogs exposure to a 5X dosage of test material was associated with a slight mean weight decrease in the period from Day -3 to Day 7.

While Group I puppies showed a greater mean weight gain in the period from Day -3 to +7 than Groups II and III, their mean weight gain/day in the subsequent period from Day 7 to 14 (0.053 kg/day) was comparable to the mean weight gains from Day -3 to +7 for Groups II (0.033 kg/day) and III (0.047 kg/day). Group III puppies also showed a greater mean weight gain in the period from Day -3 to 7 than did Group II puppies. There is no indication then that exposure to the test material affected body weight gain in puppies.

Puppies in Groups II and III showed lower mean food consumption values on Days 0 and 1 relative to their controls. This has to be considered as treatment-related. A similar effect in the adults was not evident.

No effects were noted on hematological or clinical chemistry parameters.

While the Guidelines for this type of study state that the targeted adequate margin of safety is 5X, it is also stated that: "Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)." The test material was not tested at 3X and effects were noted at 5X. However, the

effects noted at 5X, including ocular discharge (also noted in one puppy dosed at what was essentially 1.5X) and salivation were minimal (most occurrences of both ocular discharge and salivation were described as "very slight.") and reasonably transient. It is noteworthy that no systemic neurological signs (such as tremors or ataxia) were observed, and the salivation may have been due to ingestion of small amounts of test material from licking or biting the application area. In addition, the performing laboratory has demonstrated in the past extremely meticulous reporting of observational data in companion animal safety studies, and it is quite likely that these observations would not have been reported from some of the other laboratories which conduct this type of study.

For local dermal effects, one puppy treated at what was essentially a 7.5X dose level showed subsequent shoulder lesions and was noted to scratch this area frequently. Dermal exposure to pyrethroids can cause a burning and/or itching sensation at the application site, and this has to be considered an effect (unless the registrant can provide additional information demonstrating otherwise). However, this was an isolated case, and the three adult dogs treated with 3 unit doses/application with a total of 5 applications (for a total of fifteen 1.5-mL ampules in all) did not show a similar response.

However, one area of concern is that the 1.5 mL ampules (the only size tested in this study) delivered only an average of only 1.17 mL of test material, and the registrant is proposing packaging this product in 3.0 and 4.5 mL (as well as 1.0 and 1.5 mL) tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2 x 1.17) mL and the 4.5 mL tubes deliver no more than 3.51 (3 x 1.17) mL.

This study is classified as **Acceptable** as a companion animal safety study (OPPTS 870.7200) for puppies (12 weeks and older) and adult dogs. **It is concluded that there is an adequate margin of safety (at least 5X) between the exposure associated with the proposed use level for this formulation in dogs and that at which significant adverse systemic effects (not seen in this study, but which might include ear twitching, muscle tremors, drooling) may occur.** For dermal effects an effect was observed in one puppy in Group III (treated at essentially a 7.5X dose level), but in none of the other dogs (including the puppies in Group II), indicating a reasonably low potential for this effect in dogs treated at the proposed use level.

COMPLIANCE: Signed and dated Quality Assurance (p. 4), [No] Data Confidentiality (p. 2), and Good Laboratory Practice Compliance (p. 3) Statements were present.

I. MATERIALS

A. MATERIALS

1. Test material: Cyphenothrin-IGR Spot-on for Dogs, with a label declaration for active ingredients of RS-Gokilaht [=Cyphenothrin] (40.00%) , S-Methoprene (3.00%), and Nyiar (2.00%). According to a certificate of analysis on p. 47 of MRID 46166108 the respective analytical values were 39.87%, 3.00% and 2.00%. Packaged in unit dose ampules containing 1.5 mL.
   Description: A liquid;
   Lot No.: #1683B
   Storage: Room Temperature

2. Administration: Topical (spot-on)

3. Vehicle control: X-5699-03 (Placebo Control); From Study 0310: Lot #03390A0100. liquid which was stored at room temperature.

4. Test animals
Species: Dog
Breed: From p. 9 of MRID 46166108: "Beagles and other breeds..."
Ages and weights at study initiation: "Animals were at least 3 months old at dosing. There were 3 animals from each group in each of the following weight ranges: <15, 15-33, 34-65 and >65 pounds (<6.8, 6.8-15, 15.1-29.5 and >29.5 kg). All dogs less than 15 pounds were pups that were 12 weeks old at dosing." [Note by reviewer: The alkaline phosphatase measurments from Dog 2854F (controls), 3085M (Group II) and 2156M (Group III) were relatively high - refer to pp. 32-34 - suggesting these were fairly young dogs too].
Sources: Butler Farms (Clyde, NY), Martin Creek Kennels (Wiliford, AR), Ridglan Farms (Mt. Horeb, WI) and STILLMEADOW, Inc.
Housing: Individually in kennels measuring 3' x 5.5'.
Diet: PMI Canine High Density Diet 5L18.
Water: Tap water, *ad libitum*
Environmental conditions:
Temperature: 22° ± 3°C
Humidity: 30 - 70%
Air changes: 10 - 12/hr
Photoperiod: 12 hr dark/12 hr light
Acclimation period: 2 weeks

II. STUDY DESIGN

A. IN LIFE DATES

From the report cover: study initiation date: 13 August 2003; study completion date: 20 October 2003.

B. ANIMAL ASSIGNMENT/ DOSAGE AND ADMINISTRATION

There were a total of 12 dogs per dosage group. Group 1 (1X vehicle; note: observation schedule on p. 16 of MRID 46166108 is the same for Groups 1 and 2, consistent with a single application of placebo on dogs in Group 1) consisted of 9 males and 3 females; Group II (1X) consisted of 5 males and 7 females, and Group III (5X) consisted of 8 males and 4 females. Assignment was on the basis of weight. From p. 10 of MRID 46166108: "Animals selected for testing were randomly assigned to three groups... Since there were three dose sizes (based on animal body weight) to be used in each treatment group, three dogs of each weight range were included in each group. The weight ranges were <15, 15-33, 34-65 and >65 pounds (<6.6, 6.8-15, 15.1-29.5 and >29.5 kg). The dogs <15 pounds were 3-month old puppies."

From p. 10 of MRID 46166108: "The test substance and placebo were applied to the skin in a line along the spine starting at the back of the neck. The test substance was supplied in unit dose plastic tubes, each containing 1.5 mL and were administered to each animal according to its body weight. The placebo control substance was provided in bulk. On Day 0, a label dose (1X) of the test substance was administered to each Group II animal according to body weight. Group III animals received the test substance at five times the label dose (5X) administered as single doses once every hour for 5 hours. The single dose volumes were: dogs <15 pounds, 1.5 mL (one unit dose); dogs 13 [15?]-33 pounds, 1.5 mL (one unit dose); dogs 34-65 pounds, 3 mL (two unit doses); and dogs >65 pounds, 4.5 mL (three unit doses). Group I was treated with the placebo control material in a volume equivalent to that of the normal label dose of the test substance less the volume of that dose that was occupied by the active ingredients [or approximately

55% of a normal 1X dose volume]..."

TABLE 1. Study design							
Group & Weight Range (kg)		Number of dogs or puppies		Cumulative Dose/dog			Number of applications
		Male	Female	Total/Dog	Mean mL/kg	Mean Dosage Cyphenothrin (mg/kg)[d]	
I (control)	<6.6[a]	3	0	0.83 mL[b]	0.16[b]	0	1
	6.8-15	1	1	0.83 mL[b]	0.08[b]	0	
	15.1-29.5	2	2	1.65 mL[b]	0.09[b]	0	
	>29.5	3	0	2.48 mL[b]	0.07[b]	0	
II (1X)	<6.6[a]	1	2	1.17 mL[c]	0.28[c]	112[d] (121][e]	t
	6.8-15	1	2	1.17 mL[c]	0.09[c]	36[d] (39][e]	
	15.1-29.5	1	2	2.34 mL[c]	0.12[c]	48[d] [52][e]	
	>29.5	2	1	3.51 mL[c]	0.11[c]	42[d] [45][e]	
III (5X)	<6.6[a]	1	2	5.85 mL[c]	1.26[c]	503[d] [543][e]	5
	6.8-15	0	2	5.85 mL[c]	0.51[c]	207[d] [224][e]	
	15.1-29.5	3	1	11.7 mL[c]	0.64[c]	255[d] (275][e]	
	>29.5	3	0	17.55 mL[c]	0.50[c]	199[d] [215][e]	

Data calculated from information on p. 14-15 in MRID 46166108.
[a] Puppies
[b] Placebo
[c] Test material (with actives); amount delivered based on 1.17 mL/application.
[d] Based on a specific gravity for the test material of 1.00 g/mL (consistent with the calculations for dosage as reported on pp. 14-15 of MRID 46166108) and based on 1.17 mL delivered/tube.
[e] Based on a specific gravity of 1.08 g/mL
Note: According to the CSF the specific gravity of the proposed product is about 1.08; assuming the product contains 40% Cyphenothrin then 1.5 mL would be 1.62 g and would contain 648 mg of Cyphenothrin. The calculations of dosage of Cyphenothrin in the report (see p. 14-15 of MRID 46166108) appear to be based on a specific gravity for the proposed product of about 1.00. Example: Dog 3067 F weighing 4.2 kg received one 1.5 mL dose of the product and this is reported as a dosage of 142 mg/kg Cyphenothrin. 142 mg/kg x 4.2 kg = 596.4 mg; dividing this by 0.3987 (the analytical percentage) gives 1496 mg (= 1.496 g) total product applied. However, in Appendix G (see p. 52 of MRID 46166108) it is stated that the unit dose containers did not deliver the entire target dose of 1.5 mL, as there was a mean delivered volume of 1.17 mL. A statement in Appendix G ("...5X dose rates ranged from 494 to 630 mg/kg for the smallest subjects.") is consistent with delivery of 1.17 mL/dose and a specific gravity of about 1.08 g/mL.

C. DOSE SELECTION RATIONALE

According to the proposed label this product will be packaged in unidose 1.0, 1.5, 3.0 and 4.5 mL applicator tubes. These correspond to single treatments for dogs weighing 15 lbs and under, 15-33 lbs, 33-66 lbs and >66 lbs. However, in this study, Group 2 (1X) dogs (puppies) weighing less than 15 lbs received 1.5 mL (instead of 1.0 mL), while Group 3 (5X) dogs (puppies) weighing less than 15 lbs received 5 x 1.5 mL = 7.5 mL (instead of 5 x 1.0 mL = 5.0 mL).

D. EXPERIMENTAL DESIGN

From p. 10 of MRID 46166108: "Each animal was observed at 1, 2, 3 and 4 hours following dosing on Day 0 and then twice daily [AM and PM] for the duration of the study. Group III animals were also observed between the hourly dosings. Each animal was examined for signs of any pharmacologic and/or toxicologic effects. Only abnormalities were recorded."

Individual dogs were weighed on Days -7, -3, 7 and 14.

Individual food consumption was measured daily by measuring the amount of food given to each dog in the morning and subtracting the amount of food left at the end of the day.

Baseline blood samples were collected from each dog on Day -7 by jugular venipuncture following an overnight fast. Blood samples were also similarly collected on Day 1.

E. PATHOLOGICAL PARAMETERS

Blood samples were collected on Study Days -7, and 1 by jugular venipuncture following an overnight fast. The CHECKED (X) parameters were examined:

a. Hematology

X		X	
X	Hematocrit (HCT)*	X	Leukocyte differential count*
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count		Reticulocyte count
	Blood clotting measurements		
	(Thromboplastin time)		
	(Clotting time)		
X	(Prothrombin time [PT])*		
X	(Activated partial thromboplastin time [APTT])*		
	Erythrocyte morphology		

*Recommended in OPPTS 870.7200 Guidelines.

b. Clinical chemistry

X	ELECTROLYTES	X	OTHER
X	Calcium*	X	Albumin (Alb)*
X	Chloride*	X	Blood creatinine (Crea)*
	Magnesium	X	Blood urea nitrogen (BUN)*
X	Phosphorus*		Total Cholesterol
X	Potassium*	X	Globulin (Glob)*
X	Sodium*	X	Glucose (Gluc)*
		X	Total and direct bilirubin (T Bil & D Bil)*
	ENZYMES	X	Total serum protein (TP)*
X	Alkaline phosphatase(ALPor ALK)*		Triglycerides
	Cholinesterase(ChE)		Serum protein electrophoresis
	Creatine kinase	X	Albumin/Globulin (A/G) ratio
	Lactic acid dehydrogenase(LDH)		
X	Serum alanine aminotransferase (ALT or SGPT)*		
X	Serum aspartate aminotransferase(AST or SGOT)*		
	Gamma glutamyl transferase(GGT)		
	Amylase		
	Glutamate dehydrogenase		

*Recommended in OPPTS 870.7200 Guidelines.

F. STATISTICS

The statistical report is found in Appendix G. It consists of a 6-page document (pages 48-53 of MRID 46166108). From p. 51 of MRID 46166108: "The data generated by the test facility...were statistically analyzed by Student's "t" test, assuming equal variances, using the statistical program in Microsoft Excel, version 97-SR-1... Since cyphenothrin is potentially the most toxic component of the product (pyriproxyfen and methoprene are known to be virtually mammalian-inert) cyphenothrin dosage was the focus. To ensure that some of the test subjects were treated at or above the target maximum dose rate of 100 mg of cyphenothrin per kg body weight, the 12-week-old Beagle pups were treated with the next higher unit dose volume. Although weighing between 9 and 11 lb at treatment, for which the proposed label dose rate is one dose of 1 mL, these pups received one 1.5 mL unit dose. To validate the dosage delivered to the principals, the expelled contents of six 1.5 mL unit dose containers were each weighed..." [Note: the report text then refers to Table 1.1, which is not present in the report]. From p. 52 of the report: "The dose validation data (Table 1.1) indicated that the unit dose containers, if filled at the target dose volume of 1.5 mL, were not capable of delivering the entire target volume (mean volume delivered was 1.17 mL).

G. DISPOSITION OF ANIMALS

Not stated. According to the OPPTS 870.7200 Guidelines: "Routine sacrifice or necropsy is not required for surviving animals."

H. COMPLIANCE

Signed and dated Quality Assurance [p. 4], [No] Data Confidentiality [p. 2], and Good Laboratory Practice (GLP) Compliance [p. 3] Statements were present.

III. RESULTS

A. EXPOSURE LEVELS

The dose per 1.17 mL application (based on a product specific gravity of 1.08 g/mL) is 1.264 g. Since the test material contained (by analysis) 39.87% Cyphenothrin, 3.00% S-Methoprene and 2.00% Nylar, each 1.17 mL dose then contained 0.504 g (=504 mg) Cyphenothrin, 0.038 g (=38 mg) S-Methoprene and 0.025 g (=25 mg) Nylar. For Group II (1X) mean cumulative Cyphenothrin dosages were: puppies (<6.6 kg): 121 mg/kg; dogs 6.8-15 kg: 39 mg/kg; dogs 15.1-29.5 kg: 52 mg/kg; and dogs >29.5 kg: 45 mg/kg. For Group III (5X) dosages were: puppies (<6.6 kg): 543 mg/kg; dogs 6.8-15 kg: 224 mg/kg; dogs 15.1-29.5 kg: 255 mg/kg; and dogs >29.5 kg: 215 mg/kg. Refer to Table 1 of this DER. B. MORTALITY

There was no mortality, with all dogs surviving the 14-day observation period.

C. CLINICAL SIGNS

In the observation period immediately following treatment, no clinical signs of systemic toxicity were observed in Group I (controls). In Group II (1X) animal 3074 (a male pup weighing 4.1 kg) showed very slight ocular discharge from both eyes at 4 hours post-dose. In Group III (5X) four dogs (including all 3 puppies) showed very slight to moderate ocular discharge from one or both eyes in the period from one hour to 8 hours post-dosing. In addition, five dogs (including one puppy) showed very slight to moderate salivation during this period (in two dogs it was classified as very slight). Very slight salivation occurred in one animal at 1 hour (i.e., presumably following a single dosage of test material), and in two others it was first noted at 3 hours (after 3 application treatments)

Slight to moderate green ocular discharge (both eyes) was observed in one control puppy in the period from Day 1 to Day 6, and then again in this puppy from Day 10 to Day 15. No ocular discharge was observed in Group II in the period from Day 1 to Day 15. One Group III puppy showed clear ocular discharge from the left eye on Days 1 and 2, while an adult dog showed clear ocular discharge from the left eye from Day 1 through Day 6, then again from Day 13 through Day 15.

TABLE 2. Adverse Effects Observed in Dogs Treated with Cyphenothrin-IGR Spot-on In the Period Immediately Following Treatment[a]

Parameter	Group I (Control)	Group II (1X)	Group III (5X)
Ocular discharge - one or both eyes in the immediate post-dosing period	0[0]	1[1/48]	4[12/96]
Salivation	0[0]	0[0]	5[18/96]
Soft stool	0[0]	0	2[2/96]
Spiked greasy hair at application site in the immediate post-dosing period	0[0]	2[2/48)	0[0]

[a]Data taken from Table 2 (p. 15) of MRID 46166108.

From p. 11 of MRID 46166108: "Five of the Group II [1X] animals exhibited greasy spiked fur and/or white deposits at the dose site through Day 3. The only other observation noted in this group was moderate white foamy vomit in one dog on Day 8. In Group III, greasy and/or spiked fur and/or white deposits were seen through Day 1 in two dogs, through Day 3 in three dogs, through Day 6 in three dogs and [from Day 5] through Day 15 in one dog. Other observations included slight clear ocular discharge through Day 2 and shoulder lesions through Day 15 in one animal (the dog was observed to scratch the irritated area frequently), and slight to moderate diarrhea on Days 3 and 4 in another animal. Another dog had very slight to moderate clear ocular discharge through study termination with slight to moderate redness around the eye on Days 3-6. One dog exhibited slight salivation on Day 1 and moderate diarrhea on Day 14, and another had a lesion on the back on Days 7-15."

The Group III dog with the lesions on the shoulder (from p. 18: "both sides") from Day 5 through 15 was 3070M (a male puppy), treated with five 1.5 mL applications, while the Group III dog with the lesion on the back (Days 7-15) was 2853F (a female adult) also treated with five 1.5 mL applications.

D. BODY WEIGHT AND WEIGHT GAIN

From p. 12 of MRID 46166108: "The average weight gain[s] for Groups I, II and III were 1.1, 1.0 and 0.6 kilograms, respectively. There were no significant differences among groups, and no dose related responses."

The values in Table 3 are calculated from individual body weight data (p. 14-15 of MRID 46166108):

TABLE 3. Mean Body Weights for Dogs by Group

Group	kg ± S.D.				Mean Wt change Day -3 to 7	Mean Wt change Day -3 to 14
	Day -7	Day -3	Day 7	Day 14	kg ± S.D.	kg ± S.D.
I (Controls) puppies	4.63 ± 0.50	5.07 ± 0.93	6.13 ± 1.01	6.50 ± 1.10	1.07 ± 0.15	1.43 ± 0.31
I (Controls) adults	21.87 ± 9.93	22.34 ± 10.26	22.86 ± 10.90	23.31 ± 11.15	0.51 ± 0.87	0.97 ± 1.00
II (1X) puppies	4.80 ± 1.14	4.17 ± 0.06	4.50 ± 0.10	4.97 ± 0.31	0.33 ± 0.15	0.80 ± 0.36
II (1X) adults	21.64 ± 9.61	21.90 ± 9.16	22.53 ± 10.29	22.91 ± 10.29	0.41 ± 1.36	1.01 ± 1.61
III (5X) puppies	4.67 ± 0.71	4.63 ± 0.57	5.10 ± 0.70	5.63 ± 0.50	0.47 ± 0.15	1.00 ± 0.10
III (5X) adults	22.18 ± 10.00	22.38 ± 10.35	22.18 ± 10.40	22.86 ± 10.68	-0.20 ± 0.32	0.48 ± 0.58

Values calculated from data on p. 14 and 15 of MRID 46166108.

The possibility exists that there was a switch of puppies (or their bodyweights) as pup 3073M (assigned to controls) weighed 4.1 kg on day -7 but 6.1 kg on day -3, while pup 3074M (assigned to Group II or 1X) weighed 6.1 kg on day -7 but 4.1 kg on day -3. However, because this switch would have occurred before the dogs were treated, there would have been no impact on the study results.

The only group in which adults showed a mean weight loss between days -3 and +7 was Group III. The incidences of adult dogs showing weight losses between days -3 and +7 were the following: Group I: 3/9; Group II: 4/9; Group III: 6/9. It is concluded then that for adult dogs exposure to a 5X dosage of test material was associated with a slight mean weight decrease in the period from Day -3 to Day 7.

While Group I puppies showed a greater mean weight gain in the period from Day -3 to +7 than Groups II and III, their mean weight gain/day in the subsequent period from Day 7 to 14 (0.053 kg/day) was comparable to the mean weight gains from Day -3 to +7 for Groups II (0.033 kg/day) and III (0.047 kg/day). Group III puppies also showed a greater mean weight gain in the period from Day -3 to 7 than did Group II puppies. There is no indication then that exposure to the test material affected body weight gain in puppies.

TABLE 4. Mean Body Weight Gains for Puppies				
	Day -3 to +7	Day -3	Mean Pup Wt. Gain kg/Day Day -3 to +7	Mean Pup Wt. Gain kg/Day Day 7 to 14
I (Controls) puppies	1.07 ± 0.15	0.37 ± 0.15	0.107	0.053
II (1X) puppies	0.33 ± 0.15	0.47 ± 0.21	0.033	0.067
III (5X) puppies	0.47 ± 0.15	0.53 ± 0.25	0.047	0.076

Values calculated from data on p. 14 and 15 of MRID 46166108.

E. FOOD CONSUMPTION

Puppies in Groups II and III showed lower mean food consumption values on Days 0 and 1 relative to their controls. This has to be considered as treatment-related. A similar effect in the adults was not evident.

TABLE 5. Mean Diet ± S.D. (g) Consumed by Dog/Group by Day							
Group	Day -1	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5
I (Controls) puppies	227 ± 40	267 ± 14	263 ± 17	279 ± 27	315 ± 27	252 ± 41	275 ± 0
I (Controls) adults	431 ± 129	475 ± 131	525 ± 110	496 ± 138	504 ± 166	313 ± 173	496 ± 146
II (1X) puppies	193 ± 7	122 ± 3	89 ± 17	239 ± 45	200 ± 81	165 ± 11	209 ± 15
II (1X) adults	384 ± 218	387 ± 202	339 ± 248	410 ± 207	435 ± 216	310 ± 177	418 ± 192
III (5X) puppies	234 ± 27	85 ± 0	98 ± 82	201 ± 69	178 ± 51	167 ± 98	191 ± 0
III (5X) adults	445 ± 141	497 ± 122	379 ± 207	452 ± 175	435 ± 159	322 ± 236	437 ± 122

Values calculated from data on p. 26-29 of MRID 46166108.

F. HEMATOLOGY

From p. 12 of MRID 46166108: "The hematology values were within normal limits except for platelet counts, prothrombin time and/or activated partial thromboplastin time. These values were significantly elevated in all groups, including the placebo group, and therefore were not dose related."

There were no indications of any treatment related effects on hematology parameters. Alkaline phosphatase activity was elevated for puppies in all groups (and was usually above the reference range of 10-150 IU/L), but this is normal for puppies.

G. CLINICAL CHEMISTRY

There were no indications of any treatment related effects on clinical chemistry parameters. As indicated on p. 12 of MRID 46166108 clinical chemistry results "were within normal limits in males and females and the few significant differences among male or female means in any group or between group means did not appear to be related to treatment with the test substance."

H. NECROPSY FINDINGS

As there were no mortalities, there were no necropsy findings.

IV. DISCUSSION

Possible effects related to exposure to the test material included ocular discharge (seen in both eyes of one puppy in Group II at 4-hours post-dosing; classified as very slight; seen in 3 puppies and one adult in Group III in the period from one hour to eight hours following the first dose. In all 3 puppies ocular discharge, when it occurred during this period, was described as very slight. In the adult there was progression to a red, irritated, watery left eye at 8 hours following the first dosage. In addition, very slight to moderate salivation was noted in five dogs (including two puppies) of Group III in the one to eight hours following treatment. Salivation was seen in one adult (#3080, a 32.2-kg male receiving three 1.5-mL doses at each application) at the one hour observation (i.e., presumably one hour after the first treatment), and very slight salivation was seen in this one dog at 3 and 4 hours [following the first dosage], and then moderate salivation was seen at 8 hours. However, no effects ["No Observable Abnormalities"] were then seen in this dog for the remainder of the 14-day observation period.

Adult dogs dosed at the 5X level tended to show a slight mean weight loss in the week following treatment, although there was no indication of an effect on food consumption.

There was no indication of an effect on body weight in puppies at the 1X and 5X dose levels [actually 1.5X and 7.5X dose levels], although their mean food consumption levels for days 0 and 1 were noticeably lower than concurrent values of their controls as well as their own pre-exposure food consumption.

While the Guidelines for this type of study state that the targeted adequate margin of safety is 5X, it is also stated that: "Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)." The test material was not tested at 3X and effects were noted at 5X. However, the effects noted at 5X, including ocular discharge (also noted in one puppy dosed at what was essentially 1.5X) and salivation were minimal (most occurrences of both ocular discharge and salivation were described as "very slight.") and reasonably transient. It is noteworthy that no systemic neurological signs (such as tremors or ataxia) were observed, and the salivation may have been due to ingestion of small amounts of test material from licking or biting the application area. In addition, the performing laboratory has demonstrated in the past extremely meticulous reporting of observational data in companion animal safety studies, and it is quite likely that these observations would not have been reported from some of the other laboratories which conduct this type of study.

For local dermal effects, one Group III puppy (treated at what was essentially a 7.5X dose level) showed subsequent shoulder lesions (from day 5 through 15) and was noted to scratch this area frequently. Dermal exposure to pyrethroids can cause a burning and/or itching sensation at the application site, and this has to be considered an effect (unless the registrant can provide additional information demonstrating otherwise). However, this was an isolated case, and the three adult dogs treated with 3 unit doses/application with a total of 5 applications (for a total of fifteen 1.5-mL ampules in all) did not show a similar response.

However, one area of concern is that the 1.5 mL ampules (the only size tested in this study) delivered only an average of only 1.17 mL of test material, and the registrant is

proposing packaging this product in 3.0 and 4.5 mL (as well as 1.0 and 1.5 mL) tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2 x 1.17) mL and the 4.5 mL tubes deliver no more than 3.51 (3 x 1.17) mL.

This study is classified as **Acceptable** as a companion animal safety study (OPPTS 870.7200) for puppies (12 weeks and older) and adult dogs. **It is concluded then that there is an adequate margin of safety (at least 5X) between the exposure associated with the proposed use level for this formulation in dogs and the dose at which significant adverse systemic toxicological effects (not seen in this study, but which might include ear twitching, muscle tremors, drooling) may occur.** For dermal effects an effect was observed in one puppy in Group III (treated at essentially a 7.5X dose level), but in none of the other dogs in this study (including the puppies in Group II), indicating a reasonably low potential for this effect in dogs treated at the proposed use level.

STUDY DEFICIENCIES: The test material was not tested at 3X and effects were noted at 5X. However, the effects noted at 5X, including ocular discharge (also noted in one puppy dosed at what was essentially 1.5X) and salivation were minimal (most occurrences of both ocular discharge and salivation were described as "very slight."). In addition, the performing laboratory has demonstrated in the past extremely good reporting of observational data, and it is quite possible that what was reported in this study would not have been reported from some of the other laboratories which conduct this type of study.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D305948
2. **PC CODES:** 129013 Cyphenothrin, 129032 Pyriproxyfen, 105401 Methoprene
3. **CURRENT DATE:** November 23, 2004
4. **TEST MATERIAL:** Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen)

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/Product Safety Labs (New Jersey)/Project No. 13320/20-MAY-2003	46166103	LD_{50}>2000 mg/kg. Up and down method defaulting to acute tox class method. 2/5 Sprague-Dawley derived female rats died within 24 hrs after dosage at 2000 mg/kg; two rats which survived showed reduced fecal volume, ventral staining and hypoactivity, with recovery by day 4. All survivors gained weight in the period from day 0 to 7 and again from day 7 to 14. Postmortem necropsy of rats which died showed discoloration of the lungs and intestines and fluid-filled stomachs. Findings from rats which survived to terminal sacrifice were unremarkable.	III	A
Acute dermal toxicity/rat/ Product Safety Labs (New Jersey)/Project No. 13321/20-MAY-2003	46166104	LD_{50} > 2000 mg/kg. 5M & 5F Sprague-Dawley derived albino rats were dermally exposed to 2000 mg/kg for 24 hrs; no mortality, no signs of systemic toxicity. Three males had some dermal irritation with clearing by Day 2. All rats gained wt from day 0 to 7 and from day 7 to 14. No gross abnormalities were observed at post-sacrifice necropsy.	III	A
Primary eye irritation/rabbit/ Product Safety Labs (New Jersey)/Project No. 13322/20-MAY-2003	46166105	No corneal opacity. 3/3 rabbit eyes were positive (grade 2) for conjunctival irritation at 1 and 24 hrs. All eyes clear (all scores zero) by 72 hrs.	III	A
Primary dermal irritation/rabbit/ Product Safety Labs (New Jersey)/Project No. 13323/20-MAY-2003	46166106	No edema (all scores for edema = 0). All 3 sites scored 1 for erythema at 1 hr and 2 at 24, 48 and 72 hrs. One site scored 2 for erythema on day 7 while the other two scored 1. All scores zero on dat 10. The PII (average of scores at 1, 24, 48 & 72 hrs) = 1.75	IV	A
Dermal sensitization (Buehler method)/guinea pig/Product Safety Labs (New Jersey	46166107	No indication that test material is a dermal sensitizer.	Not a sensitizer	A

Companion animal/adult dog & 12-wk old puppies/ Stillmeadow TX/Project No. 7650/03/20-OCT-2003	46166106	Three groups of dogs, each containing 9 adults & three 12-week old puppies: Group I (control) was treated with the amount of vehicle at 1X; Group II was treated at 1X (dogs 6.8-15 kg: contents from one 1.5 mL ampule; 15.1-29.5 kg: contents of two 1.5 mL ampules; >29.5 kg: contents of three 1.5 mL ampules. Puppies (<6.8 kg) were treated with contents of one 1.5 mL ampule (1.5X). Group III adults were treated at 5X (with treatments at 1-hr intervals) and Group III pups were treated at 7.5X label dose. Administration was as a spot-on and/or stripe treatment on the back. Possible systemic effects noted following administration were ocular discharge in one Group II puppy at 4 hrs post-dose and in 4 Group III animals (including all 3 puppies). Salivation was also noted in 5 Group III dogs in the period (1-6 hrs) following first administration of test meterial. Puppies (but not adults) showed of Groups II and III also showed lower mean food consumption on days 0 and 1. One Group III puppy showed shoulder lesions (presumably in the area where test material was applied) from day 5 to the end of the study and was noted to scratch this area frequently. No effects on clinical chemistry or hematology parameters. One concern is that 1.5 mL ampules delivered only 1.17 mL test material; registrant is proposing packaging this product in 3.0 & 4.5 mL tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2x1.17)mL and the 4.5 mL tubes deliver no more than 3.51 (3x1.17)mL.	N/A	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated

- [Kills & Repels brown dog ticks [(*Rhipicephalus sanguineus*)] for up to 4 weeks!]
- [Kills & Repels American dog ticks [(*Dermacentor variabilis*)] for up to 4 weeks!]
- [Apply every [4 weeks]!][1 month]
- [Up to 4 weeks of flea & tick treatment!]
- ~~Kills 100% of Fleas in 1 hour and ticks in 3 hours~~
- ~~Kills 99% of fleas and ticks after [4 weeks] [1 month]~~
- ~~Kills 100% of Fleas in 1 hour and 99% after [1 month] [4 weeks]~~
- ~~Kills 100% of Ticks in 3 hours and 99% after[1month] [4 weeks~~
- [Kills & Repels fleas and ticks for up to 4 weeks!]
- ~~[Kills & Repels mosquitoes that are vectors of west nile virus]~~
- [Waterproof formula]
- [Dogs can be bathed 24 hours after squeeze-on is applied]
- ~~[Longest lasting, quick acting]~~
- ~~Works Stronger, Lasts Longer~~

Comment [MES9]: These are heightened efficacy claims.

Comment [MES10]: No acceptable data to support mosquitoes were provided; Dogs have neither been found to be susceptible to WNV nor suitable intermediate hosts resulting in human infection by feeding mosquitoes

Formatted: Bullets and Numbering

Comment [MES11]: Comparative Claims

- [Reapply once every 4 weeks.] [Reapply monthly]
- [May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[NOTE: Text or images in [ ] on this label denotes optional statements and/or images that may be used on front, back, sides, top or bottom of carton/pack and/or tube label panels.]

ACTIVE INGEDIENTS:
Cyphenothrin (CAS # 39515-40-7).....40.0%
OTHER INGREDIENTS:.....60.0%
TOTAL:.....100.0%

[NOTE: Due to limited size of carton/pack labeling, the "Ingredient Statement" may be placed to "prominently" appear on the Back Carton/Pack label panel]

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [back] [or] [side] label panel[s] for additional precautionary statements

NET CONTENTS: [Three] [Six] [Twelve] 1.5 ml tubes, or
[Three] [Six] [Twelve] 3.0 ml tubes, or
[Three] [Six] [Twelve] 4.5 ml tubes, or
[Three] [Six] [Twelve] 6.0 ml tubes

Label Comments

a. *2517-IL Claims*

[MASTER CARTON/PACK LABEL-FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On for Dogs

ABN : Sergeant's Silver Flea and Tick Squeeze-On for Dogs

ABN: Sergeant's Silver Squeeze-On for Dogs

ABN: Sentry XFC Squeeze-On for Dogs

ABN: Sentry XFC Flea and Tick Squeeze-On for Dogs

- DO NOT USE ON CATS [Box/Icon with cat image and cross-out]
- [Pleasant fresh scent [or] Fragrance [or] "a specific fragrance(s) will be identified"]
- [Flea & Tick control for dogs and puppies over 12 weeks of age]
- [Three in one protection [Kills fleas, ticks, and mosquitoes
- [Three Way Protection [Kill fleas, ticks, mosquitoes] [for up to ~~30~~ days]
- [Three in one protection! Kills ticks, and ~~mosquitoes~~
- [Up to 4 week Flea and Tick Treatment]
- [Up to 4 week Flea and Tick Control]
- 4 week [1 month] flea, tick and ~~mosquito~~ control
- Monthly flea, tick, and ~~mosquito~~ control
- [For dogs & puppies (over 12 weeks of age) More than 9 lbs.]
- [For dogs & puppies (over 12 weeks of age) 9 to 20 lbs]
- [For dogs & puppies (over 12 weeks of age) 21 to 39 lbs]
- [For dogs & puppies (over 12 weeks of age) 40 to 60 lbs]
- [For dogs & puppies (over 12 weeks of age) 61 lbs and over]
- [Three applications (for cartons with 3 applications)] and/or [3 month supply] or [12 week supply]
- [For dogs [9 lbs and up] or [9 lbs to 20 lbs] or [21 lbs to 39 lbs] or [40 lbs to 60 lbs] or [61 lbs and over]
- [Best if used year round!]
- [Kills & Repels fleas up to [4 weeks]!]
- ~~[Kills & Repels [new] fleas in less than 1 hour!]~~
- ~~[Kills & Repels [new] ticks in less than 3 hours!]~~
- ~~[Kills mosquitoes for up to 30 days!]~~
- ~~[Kill mosquitoes (vector of West Nile Virus) for up to 30 days!]~~
- ~~[Protects against blood feeding by mosquitoes (vector of heartworm) for up to 30 days!]~~
- [Kills & Repels ticks for up to [4 weeks]!]
- [Kills & Repels deer ticks (vector of lyme disease) for up to 4 weeks!]
- [Kills & Repels ticks (including deer ticks) for up to 4 weeks!)

Comment [MES1]: [28 days][4 weeks][1 month] is the conditionally acceptable claim.

Comment [MES2]: No acceptable data to support mosquitoes were provided.

Comment [MES3]: No acceptable data to support mosquitoes were provided.

Comment [MES4]: No acceptable data to support mosquitoes were provided.

Comment [MES5]: Claims may be included, if they state "Begins to kill & repel..."

Comment [MES6]: No acceptable data to support claims against mosquitoes wereprovided.

Comment [MES7]: No acceptable data to support mosquitoes provided; Dogs have neither been found to be susceptible to WNV nor suitable intermediate hosts resulting in human infection by feeding mosquitoes

Comment [MES8]: No acceptable data to support mosquitoes provided.

[MASTER CARTON/PACK LABEL – BACK/SIDE PANELS]

Sergeant's Cyphenothrin
Squeeze-On for Dogs

[DO NOT USE ON CATS] [Box/icon with cat image and cross-out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling. FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.

HOTLINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS for emergency medical treatment information.

NOTE TO PHYSICIAN OR VETERINARIAN

Treat patient symptomatically

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, [snap or] cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 9 lbs. to 20 lbs.: [For cartons containing 1.5 ml applicator tubes] Apply one tube (1.5 ml) as a spot or strip to the dog's back between the shoulder blades.

For Dogs Weighing 21 lbs. to 39 lbs.: [For cartons containing two I.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades.] [For cartons containing one 3.0 ml applicator tube] [Apply one tube (3.0 ml) as a spot or stripe to the dog's back between the shoulder blades.]

For Dogs Weighing 40 lbs. to 60 lbs.: [For cartons containing three 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the third tube as a spot or stripe to the dog's back directly in front of the base of the tail.] [For cartons containing one tube (4.5 ml)] [Apply one tube (4.5 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.]

For Dogs Weighing 61 lbs. and Over [For cartons containing at least four 1.5 ml applicator tubes] [Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml) along the dog's back extending to directly in front of the base of the tail.] or [For cartons containing at lease two 3.0 ml applicator tubes] [Apply one tube (3.0 ml) as a spot or strip to the dog's back between the shoulder blades and apply the contents of the other tube (3.0 ml) along the dog's back extending to directly in front of the base of the tail.] [For cartons containing one tube (6.0 ml)] [Apply one tube (6.0 ml) as a spot or stripe to the dog's back between the shoulder blades.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Do not remove tube from the pack until ready to use. Store in a cool (below 25° C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

Pesticide Disposal: If empty: do not reuse this container. Place in trash or offer for recycling if available. If partially filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On for Dogs is an effective and easy to use product.] ~~[Sergeant's Cyphenothrin Sqeeze-On for Dogs has demonstrated 100% control of fleas within one day of application.]~~ [As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On for Dogs should be used as part of a [an overall] [complete] program [aimed at][to][intended to][reduce] reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

Comment [MES12]: This is a heightened efficacy claim

www.sergeants.com

Comment [MES13]: FYI, any language on the website is considered labeling because it is referenced on the label.

Made in the USA

[Sergeant's is committed to providing high quality products. If you have any questions or comments about this product, please write: Sergeant's Consumer Response: P.O. Box 540399, Omaha, NE 68154-0399.]

[In case of emergency, call 1-800-224-PETS.]

[WARRANTY: SERGEANT'S PET CARE, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENT MADE ON THIS LABEL.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703

[BAR CODE AREA]

EPA Reg. No. 2517-
EPA Est. No.

[MASTER LABEL-TUBE/APPLICATOR LABEL]

PANELS-

Sergeant's Cyphenothrin Squeeze-On for Dogs, [Box/Icon with cat image and cross-out], [1.5 ml] or [3.0 ml] or [4.5 ml] or [6.0 ml], Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN, EPA REG. NO. 2517-

Exponent

Exponent
1730 Rhode Island Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

August 19, 2005

George LaRocca
Product Manager 13
US Environmental Protection Agency
Office of Pesticide Programs (7504C)
1801 South Bell Street
Crystal Mall 2, Room 266A
Arlington, VA 22202

Re: Sergeant's Equine Squeeze-On (EPA Reg. No. 2517-84)

Dear Mr. LaRocca,

On behalf of my client Sergeant's Pet Care Products, Inc. (2637 South 158th Plaza, Suite 100, Omaha, Nebraska 68130, EPA Company Number 2517), Exponent is submitting a revised product label for the recently registered product Sergeant's Equine Squeeze-On (EPA Registration Number 2517-84). As discussed during our meeting with you on July 13, 2005, efficacy data to support the registration of Sergeant's Equine Squeeze-On was generated using a negative and a positive control. The data suggests that Sergeant's Equine Squeeze-On provided better or equal efficacy to the positive control; therefore, in order to have a level playing field, we request that the Agency allow similar label claims on the label for Sergeant's Equine Squeeze-On as those found on the label for the EPA registered positive control.

Efficacy data generated to support registration of Sergeant's Equine Squeeze-On was compared against the EPA registered product MQHP-1 Spot-On (EPA Registration Number 73510-3). MQHP-1 Spot-On contains the active ingredient permethrin at 45.0%. As previously stated, the Agency has registered MQHP-1 Spot-On with more liberal label claims than were approved for Sergeant's Equine Squeeze-On. A copy of the most recent EPA stamped approved label for MQHP-1 Spot-On is enclosed (Enclosure 1). Sergeant's efficacy data, submitted to and reviewed by EPA under MRID 46358001, support the fact that Sergeant's Equine Squeeze-On provided better than or equal control to the positive control MQHP-1 Spot-On. Please see enclosed copy of EPA review dated April 14, 2005 with the appropriate sections highlighted (Enclosure 2). Based on this data, we have revised the product label for Sergeant's Equine Squeeze-On to contain similar label claims to MQHP-1 Spot-On. These label claims are less than what we originally proposed for Sergeant's Equine Squeeze-On (Enclosure 3). We request that the Agency

review the enclosed revised label (Enclosure 4) and approve it to allow Sergeant's product to be competitive in the marketplace.

Additionally as discussed, Sergeant's plans to generate additional efficacy data to support this product registration and will submit it to EPA to address the conditions of registration.

If you have any questions, please contact me at (202) 772-4932.

Sincerely,

James Messina
Authorized Representative of
Sergeant's Pet Care Products, Inc.

Enclosures

cc: Bob Scharf, Sergeant's
Tom Miller, VRRC
Larry Nouvel, Nouvel
Carrie Daniels, Exponent
Rick Tinsworth, Exponent

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060

EPA

United States
Environmental Protection Agency
Washington, DC 20460

[ ] Registration
[ ] Amendment
[X] Other

DPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
2517-84	G. LaRocca	[x] None [ ] Restricted
4. Company/Product (Name)	**PM#**	
Sergeant's Equine Spot-On	13	

5. Name and Address of Applicant *(Include ZIP Code)*
Sergeant's Pet Care Products, Inc.
2637 South 158th Plaza, Suite 100
Omaha, NE 68130

[ ] *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

[ ] Amendment - Explain below.
[X] Resubmission in response to Agency letter dated 5/18/05
[ ] Notification - Explain below.
[ ] Final printed labels in response to Agency letter dated _____
[ ] "Me Too" Application.
[ ] Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of a revised label in response to EPA registration notice dated May 18, 2005.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify)
* *Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
[ ] Label [ ] Container		[ ]

6. Manner in Which Label is Affixed to Product [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
James Messina	Authorized Representative	202-772-4932

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title
[signature]	Authorized Representative
4. Typed Name	**5. Date**
James Messina	8-19-05

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Enclosure 1

EPA Stamped Approved Label for MQHP-1 Spot-On

73510-3 07/14/2003 1/6

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 14 2003

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MarketQuest, Inc.
c/o Mr. Lain Weatherston, Ph.D.
Technology Sciences Group Inc.
4061 North 156th Drive
Goodyear, AZ 85338

Subject: Amendment Adding Claims for Mosquitoes and Ticks
MQHP-1
EPA Registration Number: 73510-3
Your Submission, Dated April 30, 2003

Dear Dr. Weatherston:

The labeling referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, is acceptable subject to the comment listed below. Two copies of the finished labeling must be submitted prior to releasing the product for shipment. A stamped copy of the label is enclosed for your records.

1. The claims for ticks are not supported by available data. EPA has data to show that a 45% permethrin spot-on product will kill and repel ticks when applied at 9 cc. per horse; however, available data do not demonstrate conclusively that a 45% product applied at only 6 cc. per horse will kill or repel ticks. You must either delete the claims for ticks or agree to submit/cite efficacy data which support these claims.

NOTE: Since EPA has data on file demonstrating the effectiveness of 45% permethrin products for tick control when applied at 9 cc. per horse, you may retain the tick claims, provided you increase the application rate to 9 cc. per horse. If you choose this option, please submit revised draft labeling incorporating this change and required data compensation forms (i.e., Certification with Respect to Citation of Data/Data Matrix).

If you have any questions regarding this action, please contact Susan Stanton of my team at (703) 305-5218.

Sincerely,

Susan L. Stanton for

George T. LaRocca
Product Manager 13
Insecticide Branch
Registration Division (7505C)

Enclosure

3/6

MQHP-1
SPOT-ON

BITING FLY PROTECTION

- KILLS AND REPELS HORN FLIES, FACE FLIES, STABLE FLIES, HORSE FLIES, DEER FILES, BLACK FLIES, HOUSE FLIES, GNATS AND MOSQUITOES FOR UP TO 2 WEEKS
- KILLS AND REPELS BITING AND NUISANCE FLIES FOR UP TO 2 WEEKS
- KILLS AND REPELS MOSQUITOES FOR UP TO 2 WEEKS
- KILLS AND REPELS TICKS ON HORSES
- PROTECTS HORSES FROM HORN FLIES, FACE FLIES, STABLE FLIES, HORSE FLIES, DEER FILES, BLACK FLIES, HOUSE FLIES, GNATS AND MOSQUITOES FOR UP TO 2 WEEKS
- PROTECTS HORSES FROM NUISANCE AND BITING FLIES FOR UP TO 2 WEEKS
- PROTECTS HORSES FROM MOSQUITOES FOR UP TO 2 WEEKS
- PROTECTS HORSES FROM TICKS
- ONE DOSE LASTS UP TO 2 WEEKS
- ONE MONTH [TWO, THREE, FOUR MONTH] SUPPLY

FOR USE ON HORSES ONLY
NOT FOR USE ON FOALS UNDER THREE [3] MONTHS OF AGE

ACTIVE INGREDIENT	
PERMETHRIN* [CAS# 52645-53-1]	45.00%
OTHER INGREDIENT	55.00%
TOTAL	100.00% [W/W]

* Cis/trans ratio: max 55%[±] cis and min 45%[±] trans

ACCEPTED
with COMMENTS
In EPA Letter Dated:
JUL 14 2003
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 73510-3

KEEP OUT OF REACH OF CHILDREN

CAUTION

SEE BACK PANEL FOR PRECAUTIONARY STATEMENTS
READ ALL DIRECTIONS BEFORE USING THIS PRODUCT

MarketQuest Inc.
746 Walker Road, Suite 10-301
Great Falls, VA 22066

EPA Registration No. 73510 - 3 EPA Establishment No. ????

NET CONTENTS: 2 x 6 cc applicators
NET CONTENTS: 4 x 6 cc applicators
NET CONTENTS: 6 x 6 cc applicators
NET CONTENTS: 8 x 6 cc applicators

4/6

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION

Harmful if swallowed or absorbed through the skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

FIRST AID

IF SWALLOWED:
Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a poison control center or doctor.

IF ON SKIN OR CLOTHING:
Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 to 20 minutes. Call a poison control center or doctor for treatment advice.

IF IN EYES:
Hold eye open and rinse slowly and gently with water for 15 to 20 minutes. Remove contact lenses, if present, after first 5 minutes, then continue rinsing eyes. Call a poison control center for treatment advice.

HOT LINE NUMBER:
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. **You may also contact the International Poison Control Center at 1-877-757-4943**

ENVIRONMENTAL HAZARDS

This product is extremely toxic to fish. Do not apply directly to water, or areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwaters.

CHEMICAL HAZARDS

Combustible. Do not use or store near heat or open flame

STORAGE AND DISPOSAL STATEMENTS

Do not contaminate water, food or feed by storage or disposal

PESTICIDE STORAGE:	Store in a cool, dry place. Protect from freezing.
PESTICIDE DISPOSAL:	Call your local solid waste agency or [1-800-CLEANUP or equivalent organization] for disposal instructions. Unless otherwise instructed place in trash. Never pour unused product down the drain or on the ground.
CONTAINER DISPOSAL:	Do not reuse empty container. Place in trash.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

Do not use on horses intended for slaughter

Sensitivities can occur after using ANY pesticide product for animals. If signs of sensitivity occur wash area with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately. Not for use on foals under three [3] months of age

Ready to use, no dilution necessary

Hold tube in upright position, pointing away from user's face and body. Break off tip or cut with scissors. Using the cc guide marks on the tube apply MQHP-1 as follows:

1] streak 1 cc on top of the croup.
2] streak 1 cc on the forehead under the forelock; taking care to avoid the eyes and mucous membranes
3] spot 1 cc over the dorsum of the carpus (front of knee) of each front leg [2 cc total]
4] spot 1 cc over the plantar surface of the tarsus (behind the hock) of each hind leg [2 cc in total]

Place empty applicator in trash

Do not reapply for 14 days.

WARRANTY

MarketQuest Inc., warrants that this product conforms to the chemical description on the label. MarketQuest Inc., neither makes nor authorizes any agent or representative to make, any other warranty of fitness or of merchantability, guarantee or representation, express or implied, concerning this material. MarketQuest Inc's maximum liability for breach of this warranty shall not exceed the purchase price of this product. Buyer and user acknowledge and assume all risks and liabilities resulting from the handling, storage and use of this material which extend beyond the use of the product under normal conditions in accord with statements made on this label.

Enclosure 2

EPA Review Dated April 14, 2005

PRODUCT PERFORMANCE / EFFICACY REVIEW
Mark Suarez, Entomologist - IB

DATE:	14 April 2005
EPA REG. NUMBER:	2517-IU
PRODUCT NAME:	Sergeants Equine Squeeze-On
REGISTRANT:	Sergeant's Pet Care Products, Inc.
PM:	George LaRocca, PM13
REVIEWER:	Linda DeLuise
DECISION #.:	345653
DP BARCODE:	307845
ACTION:	R31
ACTIVE INGREDIENT(S):	129013, Cyphenothrin.....40.0%
TYPE:	Wipe-On (Squeeze-On) for Horses
OPPTS GUIDELINE(S):	810.1000 810.3000 810.3200
MRID:	463580001
GLP ?:	No.
SITES:	Horses; Foals >3 months of age
PESTS:	Ticks, Mosquitoes
STUDY APPLICATION RATE:	9 cc/ horse (6.6-8.3 mg/kg)
LABEL APPLICATION RATE:	1 – 9 cc Tube/ animal

STUDY SUMMARY:

The registrant has submitted four studies in support of the registration for this cyphenothrin-based wipe-on for horses. The product is to be marketed with kills and repellency claims against biting flies, mosquitoes and ticks.

The first two assays examine the efficaciousness of the subject formulation in small studies without adequate replication. There was no replication of treated horses in one study and only two treated horses in the other study. The data resulting from these pilot studies do not support claims against any pest more than one day after treatment. The efficacy of the subject product against flies in comparison to a negative control is presented in Tables 1(a) and (b).

The third submitted study tested a cyphenothrin based wipe-on for horses against a negative control and a currently registered permethrin based product. Neither the subject formulation nor the registered product performed adequately in the submitted study for claims against flies (mosquitoes, house flies, horse flies, stable flies, face flies, gnats, etc...) or ticks. The registrant also submitted a field study comparing the efficacy against nuisance flies of horses for the cyphenothrin formulation in comparison to a negative control and a positive control (Fly Ban [EPA Reg.#.73510-3]). The results of this study are presented in Table 2.

Efficacy data against the American Dog Tick, *Dermacentor variabilis*, were submitted for a cyphenothrin wipe-on, a negative control, and the Fly Ban positive control mentioned above. Based upon the data submitted (9 DAT), neither the subject product nor the registered Fly Ban performed adequately to support a claim against ticks. The mean efficacy recorded against ticks was 23 and 29%, respectively.

Data submitted in support of mosquito claims were suggestive of efficacy against mosquitoes, *Cx. quinquefasciatus*, for up to 11 DAT. The products (cyphenothrin and permethrin positive control) did not effectively repel mosquitoes, only 7 ± 7% (cyphenothrin) and 12 ± 8% (permethrin control), but 0% of the mosquitoes were observed feeding when either product was applied.

Several deficiencies are present in the submitted studies. The product was tested in one location, only a small number of animals was used, the submitted data had to be reanalyzed due to erroneous statistics presented in the report, the positive control was applied at a label rate that is lower that that which is currently approved, and claims against mosquitoes require testing of the product against a greater number of species In addition, the 810.3200 Livestock, Poultry, Fur- and Wool-Bearing Animal Treatment Product Performance Test Guidelines established product performance standards as follow:

I. Ticks.
   A minimum of 90% reduction in infestation for one week and 75% reduction in infestation for one month, based upon pre- and post-treatment counts in comparison with untreated controls.

II. Flies (includes wipe-on applications).
   A minimum of 90% reduction in infestation under continued use.

Three weeks of efficacy are claimed on the label. Neither a tick nor fly claim of this duration is supported by the data submitted by the registrant.

Trial	Treatment	Fly	DAT (Days after Treatment) 1	2	7	14	22	29
Cycle 1	Control (n=2)	Face	88	100.5	88	100.5	101.5	155.5
		House	272	272	272	272	220	263
		Stable	221.5	243	221.5	243	114.5	215
		Gnat	8	17	8	17	64.5	9
		Mean	*147.4*	*158.1*	*147.4*	*158.1*	*125.1*	*160.6*
	Cyphenothrin (n=1)	Face	100	72.4	**96.6**	70	89.2	94.2
		House	**91.1**	83.7	**90.8**	**86.8**	89.1	65.8
		Stable	73.3	67.5	88.26	**85.6**	44.1	64.6
		Gnat	**100**	**100**	**100**	**100**	84.5	22.2
		Mean	*91.1*	*80.9*	*93.92*	*85.6*	*76.7*	*61.7*

(a.)

	Treatment	Fly	DAT 1	3	8	15	22
Cycle 2	Control (n=2)	Face	101	85	102	156	64
		House	272	290	220	263	243
		Stable	243	118	115	215	42
		Gnat	17	3	65	9	13
		Mean	*158.2*	*124*	*125.5*	*160.8*	*90.5*
	Cyphenothrin (n=2)	Face	**99**	69	72	40	55
		House	85	68	73	53	72
		Stable	**95**	76	65	34	0
		Gnat	**100**	**100**	81	39	42
		Mean	***94.8***	*78.2*	*72.8*	*41.5*	*42.2*

(b.)

Table 1(a) and (b). Efficacy of Cyphenothrin product in pilot studies. Numbers in bold meet, or exceed, the product performance guideline threshold of 90% population reduction.

Treatment	Fly		DAT 1	3	8	16	22
Negative Control	Face	Mean Count/Horse	57.8	49.8	123	58.4	94.4
	House		145.6	131.2	168.2	199.2	193.2
	Stable		118	83.6	108.2	117.6	94.8
	Gnat		2	2	2.4	3.8	**6**
	Horse			0.8	4.8		0.2
	Black Horse				0.6		
	Horn					318.8	131.8
	Mean		*80.8*	*53.5*	*67.9*	*139.6*	*86.7*
Cyphenothrin Wipe-On	Face	% Reduction	82	30	22	46	0
	House		68	23	13	53	22
	Stable		62	36	1	46	0
	Gnat		**100**	**100**	50	0	42
	Horse			**100**	**96**		0
	Black Horse				**100**		
	Horn					0	0
	Mean		*78*	*57.8*	*47*	*29*	*10.7*
Permethrin Wipe-On (Positive Control)	Face	% Reduction	69	13	0	3	0
	House		16	0	0	0	16
	Stable		26	0	0	0	0
	Gnat		60	60	58	5	63
	Horse			**100**	**100**		**100**
	Black Horse				**100**		
	Horn					0	0
	Mean		*42.8*	*34.6*	*43*	*1.6*	*29.8*

Table. 2. Number of flies on horses treated with Cyphenothrin wipe-on, Permethrin wipe-on or control horses. Numbers in bold meet, or exceed, the product performance guideline threshold of 90% population reduction.

ENTOMOLOGIST'S COMMENTS AND RECOMMENDATIONS:

The registration of the subject formulation is weakly supported by the data submitted. The deficiencies noted above result in a question as to the reliability of the data. However, the data submitted in Table 1 are suggestive of product efficacy.

Conditional registration of the product with flies and mosquitoes is acceptable, if the registrant meets the following requirements:

1. Only the following label claim is acceptable:

"Repels [flies][biting flies][nuisance flies][house flies][horn flies][face flies][stable flies][deer flies][black flies][gnats] and [mosquitoes]."

This will require that the registrant

a. Remove all claims against ticks or submit or cite supporting data.
b. Remove the claim "Prevents Mosquitoes that Transmit West Nile Virus..." from the label or submit or cite supporting data.
c. Remove all "kills" claims. Data must be submitted or cited which demonstrate that the product indeed kills the associated pest(s).
d. Remove all residual efficacy claims. Data must be submitted or cited which demonstrate that the product provides lasting protection for these claims to be included on the label.
e. Remove all claims that begin "Effectively kills..."
f. The duration of product efficacy upon which this claim is based has not been supported; remove the statements:
   1) "One [Dose][Treatment] Lasts up to..."
   2) "Three [3] Weeks Supply*, or, [Six[6] Weeks..."
g. Remove the claim "Waterproof!" This claim must be support be the submission or citation of efficacy data.
h. Remove all comparative claims, including:
   1) "Quick Action & Longest Acting".
   2) "Protects against biting insects 50% Longer..."
   3) "Protects against biting insects on horses 50% Longer..."
   4) "Works 50% longer..."

2. Within one year, the registrant must submit data that meet the standards set forth in the OPPTS Product Performance Guidelines 810.3200 for horse wipe-ons. Data must be submitted for flies that are commonly nuisance pests of horses, including black flies, mosquitoes (at least 2 species), a muscid, and a tabanid.

3. Ticks may not be listed on the label. Supporting data must be submitted or cited for the inclusion of these pests.

4. Claims against mosquitoes that may transmit WNV or other disease must meet specific data requirements. The registrant is encouraged to contact the efficacy reviewer for the best approach to adding statements against vectors when an associated disease is specified.

Comment on the requirement for an animal safety study is deferred to the risk and product managers.

Enclosure
002517-00010 S767226-ER

Enclosure 3

Original EPA Approved Label for Sergeant's Equine Squeeze-On

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505C)
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20004

NOTICE OF PESTICIDE:
x Registration
____ Reregistration

(under FIFRA, as amended)

EPA Reg. Number: 2517-84

Date of Issuance: MAY 18 2005

Term of Issuance: Conditional

Sergeant's Equine Squeeze- On

Name and Address of Registrant (include ZIP Code):

Sergeant's Pet Care Products, Inc.
2637 South 158th Street
Omaha, NE 68130-1703

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA sec. 3(c)(7)(A) provided that you:

1. Submit and/or cite all data required for registration/reregistration of your product when the Agency requires all registrants of similar products to submit data; and submit acceptable responses required for reregistration of your product under FIFRA section 4.

2. The efficacy data submitted do not adequately support kill and repellent claims against biting flies, mosquitoes and ticks. Therefore within one year from the date of registration please submit data that meet the standards set forth in the OPPTS Product Performance Guidelines 810.3200 for horse wipe-ons. Data must be submitted for flies that are commonly nuisance pests of horses, including black flies, mosquitoes (at least 2 species), a muscid, and a tabanid.

3. Make the labeling changes listed below before you release the product for shipment:

a. Add the phase "EPA Registration No.2517-84 ."

Signature of Approving Official:

Date:

EPA Form 8570-6

b. Based on the limited efficacy data submitted only the following label claims are supported on a conditional basis: "Repels [flies][biting flies][nuisance flies][house flies][horn flies][face flies][stable flies][deer flies][black flies][gnats] and [mosquitoes]."

c. The following claims are not supported and must be deleted from the label: 1) All claims against ticks. Supporting data must be submitted or cited for the inclusion of these pests. 2) All "kills" claims. Data must be submitted or cited which demonstrate that the product indeed kills the associated pest(s). 3]All residual efficacy claims. Data must be submitted or cited which demonstrate that the product provides lasting protection for these claims to be included on the label. 5)The statements: "One [Dose][Treatment] Lasts up to…" and "Three [3] Weeks Supply*, or, [Six[6] Weeks…" The duration of product efficacy upon which these claims are based has not been supported. 7) The claim "Waterproof!" This claim must be supported by the submission or citation of wash-fast data. 7) All comparative claims, including:"Quick Action & Longest Acting".,"Protects against biting insects 50% Longer…","Protects against biting insects on horses 50% Longer…" and "Works 50% longer…". See CFR 40 Section 156.10(a)(5)False or misleading statements.

d. Claims against mosquitoes that may transmit West Nile Disease or other diseases must meet specific data requirements. The submitted data does not fulfill this requirement therefore these claims must be deleted from the label. You may contact the Agency for the best approach to adding statements against vectors when an associated disease is specified.

e. The proposed label should contain a Note to Physician. The following statements are suggested types of information that may be included, if applicable:- technical information on symptomatology;- use of supportive treatments to maintain life functions;- medicine that will counteract the specific physiological effects of the pesticide;- company telephone number to specific medical personnel who can provide specialized medical advice.

f. Move the statements beginning,"Do not apply this product to foals .....etc., and ending, "If signs continue consult a veterinarian immediately"., to the Directions for Use section of the labeling.

g. Revise the precautionary statement to read, " Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco."

ACUTE TOXICITY REVIEW PROFILE

STUDY	MRID	CATEGORY	CLASSIFICATION
Acute Oral	46166103	III	Acceptable
Acute Dermal	46166104	III	Acceptable
Acute Inhalation		IV	Waived
Eye Irritation	46166105	III	Acceptable
Dermal Irritation	46166106	IV	Acceptable
Dermal Sensitization	46166107	No	Acceptable

A copy of the precautionary labeling and efficacy reviews are enclosed for your information.

3. Submit two (2) copies of your final printed labeling before you release the product for shipment.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). Your release for shipment of the product constitutes acceptance of these conditions.

A stamped copy of the label is enclosed for your records.

Enclosure

[MASTER CARTON/PACKAGE LABEL - FRONT PANEL]

ACCEPTED
with COMMENTS
In EPA Letter Dated:
MAY 18 2005
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 2217-84

Sergeant's Equine Squeeze-On

Biting Fly and Mosquito Protection

[➢ Kills [and] [&] Repels Horn Flies, Face Flies, Stable Flies, Horse Flies, Deer Flies, Black Flies, House Flies, Gnats [and][&] Mosquitoes for up to [3 Weeks][21 Days]].

[➢ Kills [and][&} Repels Biting [and][&][Nuisance] Flies for up to [3 Weeks][21 Days]].

[➢ Kills [and][&] Repels Mosquitoes for up to [3 Weeks][21 Days]].

[➢ Kills [and][&] Repels [Nuisance] Mosquitoes [and][&]Biting Flies for up to [3 Weeks][21 Days]].

[➢ Kills [and][&] Repels Ticks on Horses].

[➢ Effectively Kills [and] [&] Repels Horn Flies, Face Flies, Stable Flies, Horse Flies, Deer Flies, Black Flies, House Flies, Gnats [and][&] Mosquitoes for up to [3 Weeks][21 Days]].

[➢ Effectively Kills [and][&} Repels Biting [and][&][Nuisance] Flies for up to [3 Weeks][21 Days]].

[➢ Effectively Kills [and][&] Repels Mosquitoes for up to [3 Weeks][21 Days]].

[➢ Effectively Kills [and][&] Repels [Nuisance] Mosquitoes [and][&]Biting Flies for up to [3 Weeks][21 Days]].

[➢ Effectively Kills [and][&] Repels Ticks on Horses].

[➢ Protects Horses from Horn Flies, Face Flies, Stable Flies, Horse Flies, Deer Flies, Black Flies, House Flies, Gnats [and][&] Mosquitoes for up to [3 Weeks][21 Days]].

[➢ Protects Horses from [Nuisance][and][&] Biting Flies for up to [3 Weeks][21 Days]].

[➢ Protects Horses from Mosquitoes for up to [3 Weeks][21 Days].

[➢ Protects Horses from Ticks]

[➢ Protects Horses from [Nuisance] Mosquitoes [and][&] Biting Flies for up to [3 Weeks][21 Days]].

[➢ One [Dose] [Treatment] Lasts up to [3 Weeks][21 Days]].

[➢ Three [3] Weeks Supply]*or, [Six [6] Weeks Supply]* or, [Nine [9] Weeks Supply]*, or, [12 Weeks Supply]*, or [Three [3] Months Supply]*

[➢ Waterproof[!]].

[➢ Prevents Mosquitoes that Transmit West Nile Virus from Feeding on Horses for up to [3 Weeks][21 Days]].

[➢ Kills Mosquitoes, The Vector of West Nile Virus for up to [3 Weeks][21 Days]].

[➢ Quick Action & Longest Acting].

[MASTER CARTON/PACKAGE LABEL - FRONT PANEL CONT'D]

[➢ Protects Against Biting Insects 50% Longer than Permethrin Squeeze-On's for Horses].
[➢ Protects Against Biting Insects on Horses 50% Longer than Permethrin Squeeze-On Products].
[➢ Works 50% Longer].
[➢ Works 50% Longer than Permethrin Squeeze-On Products].
[➢ Ready To Use].
[➢ Ready To Use - No Dilution Required].

{LABELING NOTES:

1) Product label may contain graphics (illustrations) depicting the product's use on horses, e.g., applying or streaking of product on horses as outlined under the "Directions For Use" Section of the product label.

2) Text or images in [ ] on this label denotes optional statements and/or images that may appear on front, back, sides, top or bottom of carton/applicator outer packaging and/or applicator labeling.

3) Due to the limited size of the carton/applicator outer packaging, the "Ingredient Statement" may need to be placed on the back carton/applicator outer packaging in order for it to appear "Prominently".

***The weeks or months supply time indicated on the label will correspond to the number of application tubes contained the carton/packaging. Each applicator tube is equal to a 3-week supply. For example, a carton containing 4 x 9 cc applicator tubes may carry a statement for "3-Months" or "12-Weeks" Supply.**

ACTIVE INGREDIENT:	
Cyphenothrin (CAS# 39515-40-7)	40.0% ✓
OTHER INGREDIENTS:	60.0%
TOTAL:	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [Back][or][Side] Label Panel[s] for Additonal Precautionary Statements

NET CONTENTS: 1 x 9 cc applicator, or
2 x 9 cc applicators, or
3 x 9 cc applicators, or
4 x 9 cc applicators, or
5 x 9 cc applicators, or
6 x 9 cc applicators, or
8 x 9 cc applicators

[MASTER CARTON/PACKAGE LABEL - BACK/SIDE PANELS]

•FOR USE ON HORSES ONLY
•DO NOT USE ON FOALS LESS THAN THREE (3) MONTHS OF AGE
•DO NOT APPLY THIS PRODUCT TO HORSES INTENDED FOR SLAUGHTER OR HUMAN CONSUMPTION

READ THE ENTIRE LABEL BEFORE EACH USE.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Harmful is swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling. FOR EXTERNAL USE ON HORSES ONLY. Do not apply this product to foals less than three (3) months of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing horses. Do Not apply this product to animals other than horses. Sensitivities may occur after using ANY pesticide product on horses. If signs of sensitivity occur bathe your horse with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

FIRST AID	
If in eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have a person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take of contaminated clothing. • Rinse skin immediately with plenty of water for 15 to 20 minutes. • Call a poison control center or doctor for treatment advice.
HOTLINE NUMBER Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS or 1-800-222-1222 for emergency medical treatment information.	
NOTE TO PHYSICIAN OR VETERINARIAN This product contains the synthetic pyrethroid, Cyphenothrin. Treat patient symptomatically.	

[MASTER CARTON/PACKAGE LABEL - BACK/SIDE PANELS CONT'D]

ENVIRONMENTAL HAZARDS

This product is highly toxic to fish and other aquatic organisms. Do not apply directly to water. Do not contaminate water when disposing of the applicator device.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Read the entire label before each use.

Do Not apply this product to horses intended for slaughter or human consumption. Do Not apply this product to foals less than three (3) months of age.

How to Apply: This product is packaged in ready to use applicator tubes and does not require dilution. Hold the applicator tube with the top end pointing up and away from face and body. Snap off or remove the applicator tube tip with scissors. Invert the applicator tube and squeeze to apply product onto the horse. Follow the "cc" guide marks on the applicator tube and apply as follows:

1. Apply 2 cc on the poll taking care to keep away from the eyes and mucous membranes.
2. Apply as a "streak", 0.5cc on each side of withers (1cc total)
3. Apply as a "streak", 1cc on each side of hindquarters (2cc total)
4. Apply as a "streak", 1cc on front of each front leg below the knee (2 cc total)
5. Apply as a "streak", 1cc on the back of each hind leg below each hock on the gaskin muscle (2cc total)

[ILLUSTRATION SHOWING HORSE & APPLICATION SITES]

Reapply every 3 weeks (21 Days) only as needed to maintain pest control.

STORAGE & DISPOSAL

Do not contaminate water, food or feed by storage or disposal.
Storage: Store in a cool, dry area preferably locked and away from children and pets. Do not allow product to freeze by storing at temperatures below 32°F (0°C). Do not store in a manner that will adversely effect the applicator tube(s) or outer packaging.
Pesticide Disposal: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.
Container Disposal: Offer for recycling or puncture and dispose of in a sanitary landfill, or incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke. You may also contact your local solid waste agency or 1-800-CLEANUP for disposal instructions.

[MASTER CARTON/PACKAGE LABEL - BACK/SIDE PANELS CONT'D]

[WARRANTY

Sergeant's Pet Care Products, Inc. (hereinafter "Sergeant's"), warrants that his product conforms to the chemical description on the label. Sergeant's neither makes nor authorizes any agent or representative to make, any other warranty of fitness of merchantability, guarantee or representation, express or implied, concerning this matter. Sergeant's maximum liability for breach of this warranty shall not exceed the purchase price of the product. Buyer and user acknowledge and assume all risks and liabilities resulting from the handling, storage and use of this material which extend beyond the use of the product under normal conditions in accord with statements made on this label.]

[Sergeant's is committed to providing high quality products. If you have questions or comments about this product, please write: Sergeant's Consumer Response; P.O. Box 540399; Omaha, NE 68154-0399.]

[In Case of Emergency, call 1-800-224-PETS.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703
www.sergeants.com

[BAR CODE AREA]

EPA Reg. No. 2517 -XX
EPA Est. No. XXXXX -XX -XXX

[MASTER LABEL - TUBE/APPLICATOR LABEL]

LABEL PANELS -

Sergeant's Equine Squeeze-On; Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%; Net Contents: 9 cc.

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN EPA REG. NO. 2517-XX

Enclosure 4

Revised Proposed Label for Sergeant's Equine Squeeze-On

Sergeant's
Equine Squeeze-On

Biting Fly and Mosquito Protection

- Kills and Repels Horn Flies, Face Flies, Stable Flies, Horse Flies, Deer Flies, Black Flies, House Flies, Gnats, and Mosquitoes for up to two weeks (14 days)
- Biting Fly Protection
- One Dose lasts up to two weeks (14 days)
- Kill and Repels Biting and Nuisance Flies for up to 2 Weeks (14 days)
- Kill Mosquitoes, The Vector of West Nile Virus for up to 2 Weeks (14 Days)
- Kills and Repels Mosquitoes for up to 2 weeks
- Protects horses from horn flies, face flies, stable flies, horse flies, deer flies, black flies, house flies, gnats and mosquitoes for up to 2 weeks (14 days)
- Protects horses from mosquitoes for up to 2 weeks (14 days)

[Labeling Notes:

1. Product label may contain graphics (illustrations) depicting the product's use on horses, e.g., applying or streaking of product on horses as outlined under the "Directions for Use" section of the label.
2. Text or images in [] on this label denotes optional statements and/or images that may appear on front, back, sides, top or bottom of carton/applicator outer packaging and/or applicator labeling.
3. Due to the limited size of the carton/applicator outer packaging, the "Ingredient Statement" may need to be placed on the back carton/applicator outer packaging in order for it to appear "Prominently".
4. The weeks or months supply time indicated on the label will correspond to the number of applicatioo tubes contained in the carton/packaging. Each applicator tube is equal to a 2-week supply. For example, a carton containing 4 x 9 cc applicator tubes may carry a statement for "2-Months" or "8-Weeks" supply.]

FOR USE ON HORSES ONLY
DO NOT USE ON FOALS LESS THAN THREE [3] MONTHS OF AGE
DO NOT APPLY THIS PRODUCT TO HORSES INTENDED
FOR SLAUGHTER OR HUMAN CONSUMPTION

ACTIVE INGREDIENT	
Cyphenothrin (CAS#39515-40-7)	40.00%
OTHER INGREDIENTS	60.00%
TOTAL	**100.00%**

KEEP OUT OF REACH OF CHILDREN
CAUTION
SEE [BACK] [SIDE] PANEL FOR PRECAUTIONARY STATEMENTS
READ THE ENTIRE LABEL BEFORE EACH USE

Sergeant's Pet Care Products
2637 South 158th Plaza, Suite 100
Omaha, NE 68130-1703

EPA Reglstration No. 2517-84 **EPA Establishment No.**

NET CONTENTS: 1 x 9 cc applicators [or]
NET CONTENTS: 2 x 9 cc applicators [or]
NET CONTENTS: 3 x 9 cc applicators [or]
NET CONTENTS: 4 x 9 cc applicators [or]
NET CONTENTS: 5 x 9 cc applicators [or]
NET CONTENTS: 6 x 9 cc applicators [or]

NET CONTENTS: 8 x 9 cc applicators [or]
NET CONTENTS: 9 x 3 cc Applicators [or]
NET CONTENTS: 6 x 4.5 cc Applicators

[Back/Side Panel(s)]

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMAN AND DOMESTIC ANIMALS

CAUTION

Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. For external use on horses only.

FIRST AID	
IF IN EYES:	Hold eye open and rinse slowly and gently with water for 15 to 20 minutes. Remove contact lenses, if present, after first 5 minutes, then cootinue rinsing eyes. Contact a poison control center for treatment advice.
IF SWALLOWED:	Call a poison control center or doctor immediately for treatmeot advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a poison control center or doctor. Do oot give anythiog by mouth to an unconscious person.
IF ON SKIN OR CLOTHING:	Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 to 20 minutes. Call a poison control center or doctor for treatment advice.
HOT LINE NUMBER: Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS or 1-800-222-1222 for emergeocy medical treatment.	
NOTE TO PHYSCIAN or VETERINARIAN: This product contains the synthetic pyrethroid, Cyphenothrin. Treat patient symptomatically.	

ENVIRONMENTAL HAZARDS

This product is highly toxic to fish and other aquatic organisms. Do not apply directly to water. Do not cootaminate water when disposing of the applicator device.

WARRANTY

Sergeant's Pet Care Products, Inc. (hereinafter "Sergeant's"), warrants that this product conforms to the chemical description on the label. Sergeant's neither makes oor authorizes any agent or representative to make, any other warranty of fitness of merchantability, guarantee or representation, express or implies, concerning this mater. Sergeant's maximum liability for breach of this warranty shall not exceed purchase price of this product. Buyer and user acknowledge and assume all risks and liabilities resulting from the handling, storage and use of this material, which extend beyond the use of the product under normal conditions in accord with statemeots made on this label.

STORAGE AND DISPOSAL

Do oot contaminate water, food or feed by storage or disposal.

Pesticlde Storage: Store in a cool, dry area preferably locked and away from children and pets. Do not allow product to freeze by storing at temperatures below 32° F (0° C). Do not store in a manner that will adversely effect the applicator tube(s) or outer packaging.

Pesticide Disposal: Wastes resulting from the use of this product may be disposed of oo site or at an approved waste disposal facility.

Container Disposal: Offer for recycling or puncture and dispose of in a sanitary landfill, or incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke. You may also cootact your local solid waste agency or 1-800-CLEANUP for disposal instructions.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Read the entire label before each use.

Do not apply this product to foals less than three (3) months of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing horses. Do not apply this product to animals other than horses. Sensitivities may occur after using any pesticide product on horses. If signs of sensitivity occur bathe your horse with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately. Do not apply this product to horses intended for slaughter or human consumption.

How to Apply: This product is package in ready to use applicator tubes and does not require dilution. Hold the applicator tube with the top end pointing up and away from face and body. Snap off or remove the applicator tube tip with scissors. Invert the applicator tube and squeeze to apply product onto the horse. Follow the "cc" guide marks on the applicator tube and apply as follows:

1. Apply 2 cc on the poll taking care to keep away from the eyes and mucous membranes
2. Streak 0.5 cc on each side of withers (1cc total)
3. Streak 1 cc on each side of hindquarters (2cc total)
4. Streak 1 cc on front of each front leg below knee (2 cc total)
5. Streak 1 cc on the back of each hind leg below each hock on the gaskin muscle (2cc total).

[Three (3cc tubes per application)
Tube 1: Poll and withers
Tube 2: Hind quarters and one front leg
Tube 3: Second front leg and both rear legs]

[Two (4.5 cc tubes per application)
Tube 1: Poll, hindquarters and one side of withers
Tube 2: Front Legs, Back Legs and other side of withers]

[INSERT PICTURE WHICH SHOWS APPLICATION SITES]

Reapply every 2 weeks (14 days) only as needed to maintain pest control.

[Sergeant's is committed to providing high quality products. If you have questions or comments about this product, please write: Sergeant's Consumer Response, P.O. Box 540399, Omaha, NE 68154-0399.]

Made in the USA for:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130-1703
www.sergeants.com

[In case of emergency, call 1-800-224-PETS]

[Bar code area]

[Tube/Applicator Label]

[Label Panels]

Sergeant's Equine Squeeze-On: Active Ingredient: Cyphenothrin 40.0%, Other Ingredients: 60.0%, Net Contents: X cc.

Read directions/precautions before using.
CAUTION: KEEP OUT OF REACH OF CHILDREN
EPA Reg. No. 2517-84

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

September 26, 2006

MEMORANDUM

SUBJECT: Cyphenothrin: Revisions for "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets (3/20/2006, D317077)"; DP Barcode: 319222, PC Code: 129013

FROM: Wade Britton, MPH, Risk Assessor/ ~~Industrial Hygienist~~
Reregistration Branch 3
Health Effects Division (7509P)

THROUGH: Christina Swartz, Branch Chief
Registration Branch 2
Health Effects Division (7509P)

TO: George LaRocca and Linda DeLuise
Insecticides Branch
Registration Division (RD) (7505P)

This document serves as a revision to the previous document, "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets (3/20/2006, D317077)." The purpose of this update is to adjust the March risk assessment to reflect changes resulting from a residential handler default assumption correction and a decision to disregard the concept of a 31-day average residue level for toddler exposure to companion animals. These factors were used in the previous risk assessment to estimate toddler residential risk estimates for postapplication exposure to cyphenothrin.

One of the default assumptions used in the previous risk assessment (D317077) for the estimation of cyphenothrin residential postapplication exposure/ risk was incorrectly identified. In the previous risk assessment, toddler short-term hand-to-mouth exposures were estimated based upon a frequency of 20 events/ hour for 2 hours/ day. While this default factor is accurate for estimating toddler oral exposure from hand-to-mouth

activity on treated indoor hard surfaces and carpet, the correct default assumption for toddler exposure from hand-to-mouth activity to treated companion animals should be based upon a frequency of 1 event/ hour for 2 hours/ day. When applied to the algorithm used to estimate toddler risk for this scenario, the margin of exposure (MOE) is altered. As was performed in the risk assessment, the resulting MOEs were combined (dermal + oral) to estimate the body burden expected from exposure to multiple routes of exposure for the scenarios. The combined MOE in the risk assessment for toddler exposure from dermal (hug) and hand-to-mouth activities to treated companion animals was estimated to be 36. The combined MOE, when corrected for default assumption, results in a combined MOE of 70. Since the recalculated combined MOE for the scenario is less than 100, as was the case in the risk assessment, toddler exposure from dermal (hug) and hand-to-mouth activities to treated companion animals continues to be of concern to HED. The default factors used for the residential postapplication assessment are taken from the HED Exposure Science Advisory Committee SOPs including the following interim changes: *SOP12: Recommended Revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments* (2/22/2001) and *SOP13: Postapplication Exposure Assessment For Children From Pet Treatments* (1/2002).

In the previous risk assessment, a 31-day average residue level concept was presented to better characterize the risk estimated for toddlers from hand-to-mouth activity to a cyphenothrin-treated dog. The cyphenothrin risk assessment team revisited the use of the 31-day average residue level estimate for toddler hand-to-mouth activity to a treated dog in the risk assessment. Ultimately, it was decided that this estimate was not appropriate based upon the timing of effects seen in the 90-day sub-chronic dog study (MRID 42717503), from which the endpoint and dose were selected. The first effects (emesis) were seen in the study on Day 0 for females and on Day 1 for males. Since effects were seen so early in the study, the most protective risk estimate is the combined MOE estimated for Day 0 and, therefore, the 31-day average should be disregarded. The 31-day average residue level was not reassessed for any changes due to correction for the default assumption.

Conclusion

The combined MOE estimated for toddler exposure from dermal activity (hug) and hand-to-mouth activities to treated companion animals, when corrected for default assumption, results in a value of 70. Since the recalculated combined MOE for the scenario is less than 100, it is of concern to HED.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

September 21, 2006

MEMORANDUM

SUBJECT: Cyphenothrin: Review of Sergeant's Pet Products, Inc. Draft Protocol, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation:" DP Barcode: 330741, PC Code: 129013

FROM: Wade Britton, MPH, Risk Assessor/ Industrial Hygienist
Reregistration Branch 3
Health Effects Division (7509P)

THROUGH: Christina Swartz, Branch Chief
Registration Branch 2
Health Effects Division (7509P)

TO: George LaRocca and Linda DeLuise
Insecticides Branch
Registration Division (RD) (7505P)

This document serves as a response to Sergeant's Pet Care Products, Inc. request that the draft protocol titled, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation," submitted as a part of, "Information to Upgrade MRID 46082302, MIRD 45869402, and MRID 45869401 (MRID 46874501); Appendix V, Specific Information to Address MRID 45869402," be reviewed by the Health Effects Division (HED). Upon review, the submitted draft protocol required some changes which are addressed in this memorandum. These changes are presented as a revised draft protocol, with a description of determined changes preceding, for use by Sergeant's Pet Care Products, Inc. to move forward with plans to fulfill HED's request for a dog spot-on study.

Changes Made for Part A. General

Upon consideration of the submitted draft pet spot-on study, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation," HED determined several changes which were deemed necessary for the protocol. Major changes, as reflected in Part A. General, are the addition of a pilot study to precede the experimental study and the division of the experimental study into two separate portions (pet hug and hand-to-mouth exposure scenarios).

As detailed in the revised protocol (A. General, # 8. Experimental Summary), a pilot study (changed to A. General, # 8. Pilot Study Summary) was determined necessary to decide upon the loading capacity of the sampling media as it pertains to the number (replicates) of petting simulations required for each time interval tested. This will reduce the number of replicates required for each time interval, while producing results representative of exposure to residues on the pet for the pet hug exposure scenario. The study director will determine at what number of simulations that loading occurs and the increase of replicate number becomes moot.

The pilot study (for use with the pet hug portion of the study only) will be conducted in the following manner. 5 beagle dogs will be treated with Gokilaht between the shoulder blades on Day 0. Each treated dog will then be sampled using a different number of petting simulations at 24 hours post-application (HED has considered how each petting simulation will be performed, this is addressed in Changes to Parts B and C). The number of petting simulations (replicates) for each treated dog will be performed for either 1 simulation, 5 simulations, 10 simulations, 15 simulations, and 20 simulations (i.e., Dog #1 will have 1 simulations performed, Dog #2 will have 5 simulations performed, etc.). 2 pre-washed cotton gloves will be worn over a 5-mil Nitrile glove. All gloves will be analyzed separately and combined for each simulation to determine the appropriate number of replicates for the experimental study. Samples will be stored and shipped in glass containers. In addition, the study director will determine if breakthrough is occurring to the Nitrile glove. The Nitrile glove will only be required to be analyzed in the experimental study if breakthrough is occurring; however, whether occurring or not, it is necessary for test participants to continue to wear the Nitrile glove under the cotton layers.

HED is requiring some changes to the experimental study, as well as the addition of the pilot study, as addressed in Part A. General, 8. Experimental Summary. It was determined that the experimental study will be divided into two portions to better analyze the exposures representative of the pet hug and the hand-to-mouth scenarios. In addition, HED determined that the sampling of multiple time periods would be beneficial for analysis of Gokilaht activity on the treated pet for the pet hug portion of the experimental study. The updated sampling time periods are as follows: prior to application, 1, 6, and 24 hours after dosing, and on Days 2, 4, 7, 14, and 28 after dosing. The pet hug experimental study will be performed using the number of simulations (replicates) which

were determined appropriate from the pilot study for the updated sampling time periods. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of glove analysis. All other variables of the test system will remain the same.

The hand-to-mouth portion of the experimental study will be conducted as follows. HED determined that a 1 simulation set repeated for 10 dogs, prior to and 24 hours after application, will be acceptable for representation of this exposure scenario. The 10 dogs required for this sample set will be a separate group from those used in the pilot study, or the other portion of the experimental study. All other variables of the test system will remain the same.

Changes to Parts B. and C.

Most of the changes in Parts B. Experimental Design and C. Analysis of Sergeant's Pet Care, Inc. draft protocol are reflective of the alterations deemed necessary by HED and explained previously in Part. A. General. The following changes will be found in HED's reviewed protocol (only the sections that have changed are outlined below):

B. Experimental Design

1. Test System – Gloves

The draft protocol recommended cotton gloves only. HED recommends two pairs of cotton gloves with a 5 mil Nitrile glove underneath be worn for all study replicates.

2. Test System – Animals

d. Quantity

The draft protocol recommends the use of 10 beagle dogs for the proposed study. After review, HED recommends the use of 25 beagle dogs total for the entire study. This total includes 5 dogs for the pilot study, 10 dogs for the pet hug portion of the experimental study, and 10 dogs for the hand-to-mouth portion of the experimental study.

6. Post-Treatment Test Sampling

Changes recommended by HED for this section have been described in detail under Changes Made for Part A. General, # 9. Experimental Study (below). A description of how the petting simulation will be performed is included in HED's revised protocol. The petting simulation will be performed in the same manner for all parts (pilot, and experimental (pet hug, hand-to-mouth) studies) of the protocol. The description, as written in the revised protocol, is as follows:

The petting simulation or stroke will be performed in a manner which has been determined to mimic normal petting actions as well as actions that may occur during a child hugging the dog. Each stroke action will involve petting in a back-and-forth motion (2 pre-washed cotton gloves over 5 mil Nitrile glove) with splayed hands. The initial motion will be the back stroke, against the grain of the fur. This will be immediately followed by a forward motion, with the grain of the fur. These motions will be repeated starting with both sides (along the ribcage) of the dog, followed by the same motion along the back (dorsally). The two sides and back, in this order, with back-and-forth motion, will account for one stroke. This sequence of motions will be required for the pilot test and the experimental studies.

C. Analysis

2. Method of Analysis

The draft protocol describes cotton and latex glove collection for analysis. HED's revised protocol is changed to reflect analysis for two pairs of pre-washed cotton gloves and the 5 mil Nitrile glove (if breakthrough is determined from the pilot study).

Draft Protocol as Revised by HED for the Proposed Pet Spot-on Study

A. General

1. Study Title: Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-on Formulation

2. Purpose: To measure the dislodgeability of the test article from the haircoats of dogs treated with a spot-on formulation containing Gokilaht

3. Regulatory Compliance: This study will be conducted in compliance with US EPA Good Laboratory Practice Standards 40 CFR 160.

All procedures must be in compliance with Animal Welfare Act Regulations. All methods can be found in STILLMEADOW, Inc. Standard Operating Procedures (SOPs).

4. Quality Assurance: The Quality Assurance Unit (QAU) will review the protocol. The study information will be entered into the Master Schedule. The study will be inspected at least once during its progress. Further inspections may be scheduled as needed to ensure the integrity of the study. Any deviations from SOPs, the Protocol, or Good Laboratory Practice Standards will be immediately reported to the Study Director and Management. The report will be audited, and a statement prepared and signed which shall specify the dates inspections were made and findings reported to Management and the Study Director.

5. Test Article: Gokilaht. Test article identification will include the name, batch number, and purity. The Sponsor will also provide information regarding safety, stability, storage conditions, and disposal. The Sponsor assumes responsibility for purity, stability, identity, synthesis methods and location of documentation.

6. Proposed Schedule: Proposed start date: XX XXX 06
Proposed end date: XX XXX 06

7. Study Director: Mel Kaminsky

8. Pilot Study
Summary: The experimental study (pet hug) will be preceded by a pilot study. The pilot study has been determined necessary in order to decide upon the loading capacity of the sampling media as it pertains to the number (replicates) of petting simulations required for each time interval tested. This should reduce the number of replicates required for each time interval, while producing results representative of exposure to residues on the pet. It will be the duty of the study director to determine what number of petting simulations is necessary to load the sampling media, or at which point increasing the number of replicates becomes moot.

To determine the appropriate number of replicates, 5 beagle dogs will be treated topically with Gokilaht between the shoulders on Day 0. Each treated dog will then be sampled using a different number of petting simulations (replicates) at 24 hours post-application. The number of petting simulations (replicates) for each treated dog will be performed for either 1 simulation, 5 simulations, 10 simulations, 15 simulations, and 20 simulations

(i.e., Dog #1 will have 1 simulations performed, Dog #2 will have 5 simulations performed, etc.). 2 pre-washed cotton gloves will be worn over a 5-mil Nitrile glove. All gloves will be analyzed separately and combined for each simulation to determine the appropriate number of replicates for the experimental study. Samples will be stored and shipped in glass containers. The study director will determine if breakthrough is occurring to the Nitrile glove. The Nitrile glove will only be required to be analyzed in the experimental study if breakthrough is occurring; however, whether occurring or not, it is necessary for test participants to continue to wear the Nitrile glove under the 2 cotton layers.

9. Experimental Study

Summary: The experimental study will consist of two separate portions, pet hug and hand-to-mouth. The pet hug experimental study will be performed using the number of simulations (replicates) which were determined appropriate from the pilot study. Using this number of simulations, 10 beagle dogs will be treated topically between the shoulder blades on Day 0. The dogs' coats will be stroked for the number of replicates determined by the pilot study for the following time periods: prior to application, 1, 6, and 24 hours after dosing, and on Days 2, 4, 7, 14, and 28 after dosing. A separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of all glove samples for a given time period (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

The hand-to-mouth portion of the experimental study will be conducted as follows. A set of 1 petting simulation replicates will be repeated for 10 dogs, prior to and 24 hours after application. The 10 dogs required for this sample set will be a separate group from those used in the pilot study, or the other portion of the experimental study. Like the pet hug portion of the experimental study, a separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of all glove samples for a given time period (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

10. Protocol Amendments: Any change or alteration in the protocol must be justified and approved by the Study Director and recorded in writing.

11. Sponsor

Audits: The Sponsor may send an authorized representative to inspect the test system and/ or data on STILLMEADOW, Inc. premises during normal working hours.

B. Experimental Design

1. Test System – Gloves	2 cotton gloves (pre-washed and verified for no impurities) with 5 mil Nitrile glove underneath
2. Test System – Animals	
a. Species:	Dogs
b. Strain/ Source:	Beagles or Mongrels; STILLMEADOW, Inc. dog colony
c. Species Justification:	The dog is the species requested by the sponsor.
d. Quantity:	25 Dogs (5 pilot study, and 20 experimental studies (10 – pet hug, 10 hand-to-mouth))
e. Age and Weight:	At least 6 months old when dosing is initiated. Weights will be approximately equal so that all dogs fall into one dosing range.
f. Identification:	Tattoos and cage cards
g. Health Status:	Normal growth, appearance, and behavior will be factors to select healthy animals for testing.
3. Animal Husbandry	
a. Cage:	Stainless steel, suspended, wire bottom cage; at least 3' x 4', or 3.5' x 5' kennel
b. Housing:	Individual
c. Food:	PMI 5L18 High Density Canine Diet or other commercial product

d. Water: Tap water; available ad libitum; water dish or automatic watering system. Municipal water supply analyzed by Texas Commission on Environmental Quality.

e. Contaminants: There are no known contaminants in the feed or water available to laboratory animals that would be expected to interfere with this study.

f. Environment: Environmental controls for the animal rooms will be set to maintain a temperature of approximately 22° ± 3°C, a relative humidity range of ~ 30 – 80%, a 12-hour light/dark cycle (regulated automatically), and room ventilation of approximately 10 – 12 air changes per hour.

4. Pretest:

a. Acclimation Period: Animals will be acclimated for a period of at least 5 days.

b. Pretest Body Weights and Observations: Animals will be weighed during the acclimation period. In-life observations will be conducted daily beginning on Day 3.

c. Pre-treatment Control Sampling: The dogs will serve as their own baseline controls by the taking of negative control samples prior to dosing. All sampling (control and test) will be done according to the stroking procedures described in Section B.6, Post-Treatment Test Sampling. There will be no continuous contemporaneous controls.

5. Test Article Administration:

a. Method of Administration: On Test Day 0, the dogs will be treated with their respective dose volume of the test formulation by administering the proper amount of the formulation from a syringe (without needle attached) as a spot or stripe to the skin on the dog's back. The dog's hair coat in the

treatment area will first be parted (using the tip of the syringe to part the dog's hair) and the dose will be applied per label instructions.

b. Justification for Method of Administration: Proposed method of treatment.

c. Dosing: Dogs will be dosed based on weight ranges indicated on the product label. Dogs weighing between 15 and 33 lbs (6.8 and 15 kg) will receive 1.5 mL as a spot or stripes to the dogs back between the shoulder blades. Dogs weighing between 33 and 66 lbs (15 to 30 kg) will receive 3.0 mL applied as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.

6. Post-treatment Test Sampling: The pilot test will be performed to determine the appropriate number of replicates for the experimental study. 5 beagle dogs will be treated topically between the shoulders on Day 0, and each will be sampled using a different number of petting simulations (replicates) at 24 hours post-application. The number of petting simulations (replicates) for each treated dog will be performed for either 1 stroke, 5 strokes, 10 strokes, 15 strokes, and 20 strokes. Pre-washed cotton gloves will be worn over 5 mil Nitrile gloves for all sampling petting simulations. Each glove (cotton and Nitrile (if determined necessary)) will be analyzed separately and combined to determine the appropriate number of replicates for the experimental study.

The petting simulation or stroke will be performed in a manner which was been determined to mimic normal petting actions as well as actions that may occur during a child hugging the dog. Each stroke action will involve petting in a back-and-forth motion (cotton gloves over 5 mil Nitrile glove) with splayed hands. The initial motion will be the back stroke, against the grain of the fur. This will be immediately followed by a forward motion, with the grain of the fur. These motions will be repeated starting with both sides (along the ribcage) of the dog, followed by the same motion along the back (dorsally). The two sides and back, in this order, with back-and-forth motion, will

account for one stroke. This sequence of motions will be required for the pilot test and the experimental studies.

The pet hug experimental study will be performed using the number of simulations (replicates) which were determined appropriate from the pilot study. Using this number of simulations, 10 beagle dogs will be treated topically between the shoulder blades on Day 0. The dogs' coats will be stroked for the number of replicates determined by the pilot study for the following time periods: prior to application, 1, 6, and 24 hours after dosing, and on Days 2, 4, 7, 14, and 28 after dosing. A separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of glove (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

The hand-to-mouth portion of the experimental study will be conducted as a set of 1 petting simulation replicates. This will be repeated for 10 dogs, prior to and 24 hours after application. The 10 dogs required for this sample set will be a separate group from those used in the pilot study, or the other portion of the experimental study. Like the pet hug portion of the experimental study, a separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of glove (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

7. Test Article Accountability:

A comprehensive inventory of test substances received and used will be kept. The test article container(s) will be weighed and/or counted when received at the facility, and a record of all test articles used will be maintained.

8. Safety Precautions:

General safety precautions as required by laboratory SOPs will be followed. A 5 mil Nitrile glove will be worn under 2 cotton gloves to ensure the safety of the technician from any dislodged test substance that might soak through the cotton gloves. The Sponsor will supply basic toxicity data on the test article to be used. However, since the toxicity of the test article is not often well characterized, the laboratory

should be conservative in setting safety procedures. The Sponsor or Sponsor's Representative shall be notified of any personnel exposures requiring a physician's examination or care.

C. Analysis

1. Transfer of Material: Each glove used in the pilot and experimental studies (pre- and post-dose sampling) will be immediately placed in a separate container and hand delivered to the laboratory to be analyzed for residue. A sample tracking form detailing animal numbers, samples, date and time will accompany each sample delivered to the chemistry department. The results of the analyses and date/time analyzed will be included in the final report.

2. Method of Analysis: All gloves (cotton and Nitrile (if determined necessary)), including those used for stroking the animals and gloves used for field fortifications will be analyzed by using the test method developed and validated by the testing facility. The methods used for extraction and analysis will be documented in the data and the final report.

3. Reference Standards: For characterization of the active ingredient in the test article, certified active ingredient will be used as the analytical reference standard.

D. Data Management

1. Records: The following records will be maintained during the study and transferred to the laboratory archives upon study termination:

a. Protocol and protocol amendments (if any)
b. Final report and amendments (if any)
c. Study correspondence
d. Animal and glove receipt data
e. Test article receipt, identification as supplied by Sponsor, preparation, administration, and disposition
f. Test animal information: number, sex, source, strain, and age and glove identification information
g. Pretest body weights
h. General clinical signs

i. Other pertinent data

2. Data Storage — All raw data, the protocol, analytical data and final report will be retained at the laboratory in the archives.

3. Data Reporting — The final report will include:

a. Statement from the Quality Assurance Unit
b. Signature of the Study Director
c. A GLP Compliance Statement signed by the Study Director
d. Names of scientific personnel involved in the study
e. Dates of study initiation and termination
f. Identification, description, preparation, and storage of the test article
g. All pertinent animal data, animal husbandry, dosing information, and observation methods as well as glove information
h. Description of the dosing and sampling procedures
i. Body weights
j. General clinical signs
k. Results of glove analysis
l. The protocol as appendix

4. Report Submission: A final report will be submitted after termination of the analytical portion of the study.

D317-12

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

September 26, 2006

MEMORANDUM

SUBJECT: Cyphenothrin: Revisions for "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets (3/20/2006, D317077)"; DP Barcode: 319222, PC Code: 129013

FROM: Wade Britton, MPH, Risk Assessor/ ~~Industrial Hygienist~~
Reregistration Branch 3
Health Effects Division (7509P)

THROUGH: Christina Swartz, Branch Chief
Registration Branch 2
Health Effects Division (7509P)

TO: George LaRocca and Linda DeLuise
Insecticides Branch
Registration Division (RD) (7505P)

This document serves as a revision to the previous document, "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets (3/20/2006, D317077)." The purpose of this update is to adjust the March risk assessment to reflect changes resulting from a residential handler default assumption correction and a decision to disregard the concept of a 31-day average residue level for toddler exposure to companion animals. These factors were used in the previous risk assessment to estimate toddler residential risk estimates for postapplication exposure to cyphenothrin.

One of the default assumptions used in the previous risk assessment (D317077) for the estimation of cyphenothrin residential postapplication exposure/ risk was incorrectly identified. In the previous risk assessment, toddler short-term hand-to-mouth exposures were estimated based upon a frequency of 20 events/ hour for 2 hours/ day. While this default factor is accurate for estimating toddler oral exposure from hand-to-mouth

activity on treated indoor hard surfaces and carpet, the correct default assumption for toddler exposure from hand-to-mouth activity to treated companion animals should be based upon a frequency of 1 event/ hour for 2 hours/ day. When applied to the algorithm used to estimate toddler risk for this scenario, the margin of exposure (MOE) is altered. As was performed in the risk assessment, the resulting MOEs were combined (dermal + oral) to estimate the body burden expected from exposure to multiple routes of exposure for the scenarios. The combined MOE in the risk assessment for toddler exposure from dermal (hug) and hand-to-mouth activities to treated companion animals was estimated to be 36. The combined MOE, when corrected for default assumption, results in a combined MOE of 70. Since the recalculated combined MOE for the scenario is less than 100, as was the case in the risk assessment, toddler exposure from dermal (hug) and hand-to-mouth activities to treated companion animals continues to be of concern to HED. The default factors used for the residential postapplication assessment are taken from the HED Exposure Science Advisory Committee SOPs including the following interim changes: *SOP12: Recommended Revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments* (2/22/2001) and *SOP13: Postapplication Exposure Assessment For Children From Pet Treatments* (1/2002).

In the previous risk assessment, a 31-day average residue level concept was presented to better characterize the risk estimated for toddlers from hand-to-mouth activity to a cyphenothrin-treated dog. The cyphenothrin risk assessment team revisited the use of the 31-day average residue level estimate for toddler hand-to-mouth activity to a treated dog in the risk assessment. Ultimately, it was decided that this estimate was not appropriate based upon the timing of effects seen in the 90-day sub-chronic dog study (MRID 42717503), from which the endpoint and dose were selected. The first effects (emesis) were seen in the study on Day 0 for females and on Day 1 for males. Since effects were seen so early in the study, the most protective risk estimate is the combined MOE estimated for Day 0 and, therefore, the 31-day average should be disregarded. The 31-day average residue level was not reassessed for any changes due to correction for the default assumption.

Conclusion

The combined MOE estimated for toddler exposure from dermal activity (hug) and hand-to-mouth activities to treated companion animals, when corrected for default assumption, results in a value of 70. Since the recalculated combined MOE for the scenario is less than 100, it is of concern to HED.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

September 21, 2006

MEMORANDUM

SUBJECT: Cyphenothrin and Etofenprox: Review and Response to, "Information to Upgrade MRID 46082302, MRID 45869402, and MRID 45869401" (MRID 46874501); DP Barcode: 330745; PC Codes: Cyphenothrin: 129013; Etofenprox: 128965

FROM: Wade Britton, MPH, Risk Assessor/ Industrial Hygienist
Reregistration Branch 3
Health Effects Division (7509P)

THROUGH: Christina Swartz, Branch Chief
Registration Branch 2
Health Effects Division (7509P)

TO: George LaRocca and Linda DeLuise
Insecticides Branch
Registration Division (RD) (7505P)

Background

This document serves as a response to Sergeant's Pet Care Products, Inc. request (MRID 46874501) to upgrade the following studies to acceptable: "Dislodgeability of Etofenprox from the Haircoat of Cats Treated with a Spot-on Formulation"(MRID 46082302), "Validation Study Comparing Dose Residue Recoverability of Etofenprox from Cotton and Latex Gloves Analysis of Data and Conclusions" (MRID 45869402), and "Amended Final Report II: Operator Exposure Assessment and Dislodgeability of Etofenprox from the Haircoat of Cats Treated with a Spot-on Formulation" (MRID 45869401). MRIDs 46082302 and 45869402 were reviewed on March 6, 2006, and the Health Effects Division (HED) determined that these studies were not suitable for risk assessment purposes due to several significant deficiencies. MRID 45869401 was reviewed on March 16, 2006 and was also determined not suitable for risk assessment purposes for many of the same deficiencies. These studies were not used in the development for the HED assessment "Etofenprox: Occupational and Residential Exposure Assessment for

Proposed Section 3 Registration on Domestic Pets (D327844)" due to deficiencies, as well as differences between certain standard assumptions in the submitted studies and those used by HED. The same Etofenprox studies were submitted by the Registrant for the HED assessment "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets (D317077)." HED also determined that the study results could not be used to support the registration of any of the cyphenothrin proposed spot-on products (2517-IL, 2517-IN, and 2517-ON). The current submission from Sergeant's Pet Care Products, Inc. is a formal request to upgrade the studies based on additional information to address the study deficiencies.

Due to the deficiencies in the aforementioned studies, the risk assessment, "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets" (D317077), used surrogate data for the estimation of residential postapplication exposure for scenarios pertaining to cyphenothrin pet spot-on products. The surrogate data were derived from a study on the dislogeability of tetrachlorovinphos from animals treated with a pump-spray treatment product (MRID 45485501). The study was previously reviewed by HED and determined to be suitable for risk assessment purposes. The dataset for this study estimates the percent available on the fur that is transferred to the hand to be approximately 5%. The 5% value from the tetrachlorovinphos dislodgeability study was used in lieu of the more conservative 20% standard value from HED's Residential Exposure SOPs 1,2,3, based on HED's determination that the tetrachlorvinphos study was more reflective of the spot-on use than the study from which the standard 20% value was derived. The 20% value was derived from a study on a shampoo product that was applied by vigorous rubbing of the treated area for an extended period of time. In using these data, HED assumed that the proposed cyphenothrin pet spot-on products are more similar to the tetrachlorovinphos product than to the shampoo product.

The residential postapplication section of the risk assessment (D317077) used the tetrachlorovinphos dislodgeability value (5%) to estimate toddler combined risk from exposures to cyphenothrin from the proposed pet spot-on uses. The combined estimated margins of exposure (MOEs) (pet hug and hand-to-mouth scenarios) for childrens' exposure to treated companion dogs are less than 100 (day zero) and, therefore, are of concern to HED. Sergeant's Pet Care, Inc. has expressed concern that the tetrachlorovinphos study, which was conducted using a pump-spray product, is not appropriate to assess the proposed spot-on formulation. If HED were to use the dislodgeability value (0.05%) from the study (MRID 45869401) submitted by Sergeant's Pet Care, Inc., the combined MOEs would be two orders of magnitude higher (well above the LOC of 100), and, therefore, not of concern to HED. However, this study, as previously mentioned, was determined not to be suitable for risk assessment purposes. While not chemical-type or use specific, the tetrachlorovinphos study was determined to be the most appropriate and protective study available for the assessment of potential risk from residential postapplication exposure to cyphenothrin from the proposed pet spot-on uses.

Previously Submitted Studies and Proposal to Upgrade the Studies

Sergeant's Pet Care, Inc. submitted dislodgeability studies (MRID 46082302 and 45869401) that were conducted with latex gloves instead of cotton gloves which would typically be used in a dislodgeability study. It is unclear to HED why the decision was made by the Registrant to perform the dislodgeability studies with a latex glove when the standard practice is the use of cotton gloves, due to their absorptive qualities. The Registrant's submitted request (MRID 46874501) cites a meeting in 2003 with the Agency in reference to this topic; however, neither the Registrant nor the Agency could locate any written documentation of the cited meeting.

Sergeant's Pet Care Products, Inc. performed a separate study, "Validation Study Comparing Dose Residue Recoverability of Etofenprox from Cotton and Latex Gloves Analysis of Data and Conclusions" (MRID 45869402) to support their decision to use a latex glove. The results of this study suggested that the use of latex gloves provided better sampling (i.e., higher recovery of residues) from the dogs than did cotton gloves; however, the study was found to be deficient. In the review completed March 6, 2006 by HED (D298228), the following limitations were described: missing information, including details regarding fortification methods; storage conditions of samples during shipping; the exact time from spike fortification to sample analysis; specific analytical methods used; the limit of quantitation (LOQ); and the sample preparation and handling of controls. Most notably, HED was concerned that both the cotton and latex glove results fell below the acceptable spike recovery range of 70-120%. Mean recovery of etofenprox ranged from 11.51% to 16.54% for cotton gloves, while mean recovery ranged from 54.47% to 67.56% for latex gloves (6 samples per matrix). Sergeant's Pet Care Products, Inc.'s submitted request (MRID 46874501) addresses a majority of the listed deficiencies. However, it does not adequately address the problem of low recoveries, a deficiency acknowledged by the Registrant. HED has determined that low mean recovery, exacerbated by a low number of samples per matrix (6 for each cotton, and latex), results in greater uncertainty than is acceptable for risk assessment purposes, particularly, since the study was conducted using latex gloves. HED's Scientific Advisory Council for Exposure (ExpoSAC) believes that cotton gloves are the most absorbent media and, therefore, should be used in this type of dislodgeability study.

The submitted request (MRID 46874501) also specifically addresses study "Dislodgeability of Etofenprox from the Haircoat of Cats Treated with a Spot-on Formulation" (MRID 46082302). Like the cotton and latex validation study, this study was found to have multiple limitations which prohibits its use for risk assessment purposes. These include: the LOQ values were not provided and residues detected below the LOQ were reported as 0; detailed information regarding the analytical methodology including extraction procedures of etofenprox from the gloves and HPLC detection methods were not provided; laboratory and field fortification spikes were not used in the study; information regarding the storage stability of the samples was not provided; method validation results indicate that the recovery of etofenprox from spiked glove samples was very low (i.e., 47 to 54%); and latex gloves were used in the study to

monitor residue transfer from cats' fur to human hands. As was the case for the previously discussed study (MRID 45869402), the current submission addresses a majority of these deficiencies. However, again HED has determined that low mean recovery results in greater uncertainty than is acceptable for risk assessment purposes. Furthermore, the validation study (MRID 45869402), which was performed to support the use of a latex glove in study MRID 46082302, was determined not to be reliable for risk assessment purposes. Finally, in the dislodgeability study no etofenprox was recovered at all from any gloves used to stroke the cat for 4 hours, 24 hours, or 2 days after treatment. It is the opinion of HED's ExpoSAC that the absence of removable, detectable residues is unlikely following pet treatment with etofenprox.

HED has concluded that Sergeant's Pet Care Products, Inc. submitted request (MRID 46874501) also fails to adequately address the deficiencies of MRID 45869401. The results of this study give a dislodgeability value of 0.05% which the Registrant has requested HED use in the risk assessment (D317077) for the available percentage of cyphenothrin for transfer to the hands. The Registrant indicates that the deficiencies for this study are the same as those for MRID 46082302 and, therefore, did not provide any additional information addressing this study specifically. While some of the deficiencies are adequately addressed by the submitted information, additional study-specific information is needed to address the remaining deficiencies. As with the other studies, the low mean recoveries and the choice of the latex glove render the study unacceptable for risk assessment purposes.

As detailed in this document, the cyphenothrin residential postapplication risk assessment (D317077) used tetrachlorovinphos surrogate dislodgeability data (5%) to estimate toddler combined risk from exposure to cyphenothrin from the proposed pet spot-on uses. Sergeant's Pet Care, Inc. stated in the submitted request (MRID 46874501) that they did not believe that it is appropriate to use an organophosphate (OP) chemical (tetrachlorovinphos) to assess exposures to cyphenothrin. The Registrant also stated that they did not agree with the use of a pump-spray study to assess a spot-on use. The arguments presented by the Registrant are considered by HED to be valid; however, the best available data were used. In order to refine the risk assessment, HED recommends that a new study (i.e., one without the deficiencies) be conducted.

Although HED determined that the tetrachlorovinphos data were the best surrogate data available, it is likely that these data overestimate residential postapplication risk due to differences between the use patterns (spray-pump vs spot-on). When a pump-spray product is applied, it goes on wet, soaking the animal's coat in the areas of treatment, with some product eventually seeping to the skin. A spot-on is applied directly to the skin (through parted coat) in a manner which results in little contact with the animal's coat. As a result of these differences, the pump-spray treatment is presumed to result in more readily available surface residues for transfer to humans than the proposed spot-on treatments. Spot-on treatments are applied directly to the animals' skin, and thought to migrate more along the skin of the animal (i.e., not the fur). Therefore, the dislodgeability estimate of 5% used for the risk assessment may be greater than would be expected from the spot-on use; however, due to the uncertainty of the Registrant's

submitted study, the result of 0.05% dislodgeability cannot be used for risk assessment purposes.

The combined estimated margin of exposure (MOE) (pet hug and hand-to-mouth scenarios) for childrens' exposure to treated companion dogs (day zero), based on the assumption of 5% dislodgeability, is 70 ("Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets" (D317077). If a slightly lower dislodgeability value (e.g., 3%) were used, the estimated combined MOE for children would be approximately 120, which is above the LOC of 100 and, therefore, not of concern to HED. While HED has provided a rationale for using the 5% value for dislodgeable residue, the most appropriate value for use in the risk assessment of the proposed spot-on uses would be determined from an acceptable cyphenothrin residue transferability study. HED understands that Sergeant's Pet Care, Inc. intends to move forward with a dog spot-on study to measure dislodgeable residues, as they have submitted a draft protocol for this study. The Registrant's draft protocol has been reviewed by HED (D330741) and suggestions have been made for how this should be performed. Furthermore, HED recognizes that the 5% value is conservative in nature and anticipates the confirmatory study may generate a value (3% or less) which would result in an acceptable combined MOE for residential postapplication risk.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
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September 21, 2006

MEMORANDUM

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2517-1W

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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September 21, 2006

MEMORANDUM

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Background

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Proposed Section 3 Registration on Domestic Pets (D327844)" due to deficiencies, as well as differences between certain standard assumptions in the submitted studies and those used by HED. The same Etofenprox studies were submitted by the Registrant for the HED assessment "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets (D317077)." HED also determined that the study results could not be used to support the registration of any of the cyphenothrin proposed spot-on products (2517-IL, 2517-IN, and 2517-ON). The current submission from Sergeant's Pet Care Products, Inc. is a formal request to upgrade the studies based on additional information to address the study deficiencies.

Due to the deficiencies in the aforementioned studies, the risk assessment, "Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets" (D317077), used surrogate data for the estimation of residential postapplication exposure for scenarios pertaining to cyphenothrin pet spot-on products. The surrogate data were derived from a study on the dislogeability of tetrachlorovinphos from animals treated with a pump-spray treatment product (MRID 45485501). The study was previously reviewed by HED and determined to be suitable for risk assessment purposes. The dataset for this study estimates the percent available on the fur that is transferred to the hand to be approximately 5%. The 5% value from the tetrachlorovinphos dislodgeability study was used in lieu of the more conservative 20% standard value from HED's Residential Exposure SOPs 1,2,3, based on HED's determination that the tetrachlorvinphos study was more reflective of the spot-on use than the study from which the standard 20% value was derived. The 20% value was derived from a study on a shampoo product that was applied by vigorous rubbing of the treated area for an extended period of time. In using these data, HED assumed that the proposed cyphenothrin pet spot-on products are more similar to the tetrachlorovinphos product than to the shampoo product.

The residential postapplication section of the risk assessment (D317077) used the tetrachlorovinphos dislodgeability value (5%) to estimate toddler combined risk from exposures to cyphenothrin from the proposed pet spot-on uses. The combined estimated margins of exposure (MOEs) (pet hug and hand-to-mouth scenarios) for childrens' exposure to treated companion dogs are less than 100 (day zero) and, therefore, are of concern to HED. Sergeant's Pet Care, Inc. has expressed concern that the tetrachlorovinphos study, which was conducted using a pump-spray product, is not appropriate to assess the proposed spot-on formulation. If HED were to use the dislodgeability value (0.05%) from the study (MRID 45869401) submitted by Sergeant's Pet Care, Inc., the combined MOEs would be two orders of magnitude higher (well above the LOC of 100), and, therefore, not of concern to HED. However, this study, as previously mentioned, was determined not to be suitable for risk assessment purposes. While not chemical-type or use specific, the tetrachlorovinphos study was determined to be the most appropriate and protective study available for the assessment of potential risk from residential postapplication exposure to cyphenothrin from the proposed pet spot-on uses.

Previously Submitted Studies and Proposal to Upgrade the Studies

Sergeant's Pet Care, Inc. submitted dislodgeability studies (MRID 46082302 and 45869401) that were conducted with latex gloves instead of cotton gloves which would typically be used in a dislodgeability study. It is unclear to HED why the decision was made by the Registrant to perform the dislodgeability studies with a latex glove when the standard practice is the use of cotton gloves, due to their absorptive qualities. The Registrant's submitted request (MRID 46874501) cites a meeting in 2003 with the Agency in reference to this topic; however, neither the Registrant nor the Agency could locate any written documentation of the cited meeting.

Sergeant's Pet Care Products, Inc. performed a separate study, "Validation Study Comparing Dose Residue Recoverability of Etofenprox from Cotton and Latex Gloves Analysis of Data and Conclusions" (MRID 45869402) to support their decision to use a latex glove. The results of this study suggested that the use of latex gloves provided better sampling (i.e., higher recovery of residues) from the dogs than did cotton gloves; however, the study was found to be deficient. In the review completed March 6, 2006 by HED (D298228), the following limitations were described: missing information, including details regarding fortification methods; storage conditions of samples during shipping; the exact time from spike fortification to sample analysis; specific analytical methods used; the limit of quantitation (LOQ); and the sample preparation and handling of controls. Most notably, HED was concerned that both the cotton and latex glove results fell below the acceptable spike recovery range of 70-120%. Mean recovery of etofenprox ranged from 11.51% to 16.54% for cotton gloves, while mean recovery ranged from 54.47% to 67.56% for latex gloves (6 samples per matrix). Sergeant's Pet Care Products, Inc.'s submitted request (MRID 46874501) addresses a majority of the listed deficiencies. However, it does not adequately address the problem of low recoveries, a deficiency acknowledged by the Registrant. HED has determined that low mean recovery, exacerbated by a low number of samples per matrix (6 for each cotton, and latex), results in greater uncertainty than is acceptable for risk assessment purposes, particularly, since the study was conducted using latex gloves. HED's Scientific Advisory Council for Exposure (ExpoSAC) believes that cotton gloves are the most absorbent media and, therefore, should be used in this type of dislodgeability study.

The submitted request (MRID 46874501) also specifically addresses study "Dislodgeability of Etofenprox from the Haircoat of Cats Treated with a Spot-on Formulation" (MRID 46082302). Like the cotton and latex validation study, this study was found to have multiple limitations which prohibits its use for risk assessment purposes. These include: the LOQ values were not provided and residues detected below the LOQ were reported as 0; detailed information regarding the analytical methodology including extraction procedures of etofenprox from the gloves and HPLC detection methods were not provided; laboratory and field fortification spikes were not used in the study; information regarding the storage stability of the samples was not provided; method validation results indicate that the recovery of etofenprox from spiked glove samples was very low (i.e., 47 to 54%); and latex gloves were used in the study to

monitor residue transfer from cats' fur to human hands. As was the case for the previously discussed study (MRID 45869402), the current submission addresses a majority of these deficiencies. However, again HED has determined that low mean recovery results in greater uncertainty than is acceptable for risk assessment purposes. Furthermore, the validation study (MRID 45869402), which was performed to support the use of a latex glove in study MRID 46082302, was determined not to be reliable for risk assessment purposes. Finally, in the dislodgeability study no etofenprox was recovered at all from any gloves used to stroke the cat for 4 hours, 24 hours, or 2 days after treatment. It is the opinion of HED's ExpoSAC that the absence of removable, detectable residues is unlikely following pet treatment with etofenprox.

HED has concluded that Sergeant's Pet Care Products, Inc. submitted request (MRID 46874501) also fails to adequately address the deficiencies of MRID 45869401. The results of this study give a dislodgeability value of 0.05% which the Registrant has requested HED use in the risk assessment (D317077) for the available percentage of cyphenothrin for transfer to the hands. The Registrant indicates that the deficiencies for this study are the same as those for MRID 46082302 and, therefore, did not provide any additional information addressing this study specifically. While some of the deficiencies are adequately addressed by the submitted information, additional study-specific information is needed to address the remaining deficiencies. As with the other studies, the low mean recoveries and the choice of the latex glove render the study unacceptable for risk assessment purposes.

As detailed in this document, the cyphenothrin residential postapplication risk assessment (D317077) used tetrachlorovinphos surrogate dislodgeability data (5%) to estimate toddler combined risk from exposure to cyphenothrin from the proposed pet spot-on uses. Sergeant's Pet Care, Inc. stated in the submitted request (MRID 46874501) that they did not believe that it is appropriate to use an organophosphate (OP) chemical (tetrachlorovinphos) to assess exposures to cyphenothrin. The Registrant also stated that they did not agree with the use of a pump-spray study to assess a spot-on use. The arguments presented by the Registrant are considered by HED to be valid; however, the best available data were used. In order to refine the risk assessment, HED recommends that a new study (i.e., one without the deficiencies) be conducted.

Although HED determined that the tetrachlorovinphos data were the best surrogate data available, it is likely that these data overestimate residential postapplication risk due to differences between the use patterns (spray-pump vs spot-on). When a pump-spray product is applied, it goes on wet, soaking the animal's coat in the areas of treatment, with some product eventually seeping to the skin. A spot-on is applied directly to the skin (through parted coat) in a manner which results in little contact with the animal's coat. As a result of these differences, the pump-spray treatment is presumed to result in more readily available surface residues for transfer to humans than the proposed spot-on treatments. Spot-on treatments are applied directly to the animals' skin, and thought to migrate more along the skin of the animal (i.e., not the fur). Therefore, the dislodgeability estimate of 5% used for the risk assessment may be greater than would be expected from the spot-on use; however, due to the uncertainty of the Registrant's

submitted study, the result of 0.05% dislodgeability cannot be used for risk assessment purposes.

The combined estimated margin of exposure (MOE) (pet hug and hand-to-mouth scenarios) for childrens' exposure to treated companion dogs (day zero), based on the assumption of 5% dislodgeability, is 36 ("Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets" (D317077). If a slightly lower dislodgeability value (e.g., 3%) were used, the estimated combined MOE for children would be approximately 120, which is above the LOC of 100 and, therefore, not of concern to HED. While HED has provided a rationale for using the 5% value for dislodgeable residue, the most appropriate value for use in the risk assessment of the proposed spot-on uses would be determined from an acceptable cyphenothrin residue transferability study. HED understands that Sergeant's Pet Care, Inc. intends to move forward with a dog spot-on study to measure dislodgeable residues, as they have submitted a draft protocol for this study. The Registrant's draft protocol has been reviewed by HED (D330741) and suggestions have been made for how this should be performed. Furthermore, HED recognizes that the 5% value is conservative in nature and anticipates the confirmatory study may generate a value (3% or less) which would result in an acceptable combined MOE for residential postapplication risk.

9517-1L

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

September 21, 2006

MEMORANDUM

SUBJECT: Cyphenothrin: Review of Sergeant's Pet Products, Inc. Draft Protocol, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation:" DP Barcode: 330741, PC Code: 129013

FROM: Wade Britton, MPH, Risk Assessor/ Industrial Hygienist
Reregistration Branch 3
Health Effects Division (7509P)

THROUGH: Christina Swartz, Branch Chief
Registration Branch 2
Health Effects Division (7509P)

TO: George LaRocca and Linda DeLuise
Insecticides Branch
Registration Division (RD) (7505P)

This document serves as a response to Sergeant's Pet Care Products, Inc. request that the draft protocol titled, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation," submitted as a part of, "Information to Upgrade MRID 46082302, MIRD 45869402, and MRID 45869401 (MRID 46874501); Appendix V, Specific Information to Address MRID 45869402," be reviewed by the Health Effects Division (HED). Upon review, the submitted draft protocol required some changes which are addressed in this memorandum. These changes are presented as a revised draft protocol, with a description of determined changes preceding, for use by Sergeant's Pet Care Products, Inc. to move forward with plans to fulfill HED's request for a dog spot-on study.

Changes Made for Part A. General

Upon consideration of the submitted draft pet spot-on study, "Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-On Formulation," HED determined several changes which were deemed necessary for the protocol. Major changes, as reflected in Part A. General, are the addition of a pilot study to precede the experimental study and the division of the experimental study into two separate portions (pet hug and hand-to-mouth exposure scenarios).

As detailed in the revised protocol (A. General, # 8. Experimental Summary), a pilot study (changed to A. General, # 8. Pilot Study Summary) was determined necessary to decide upon the loading capacity of the sampling media as it pertains to the number (replicates) of petting simulations required for each time interval tested. This will reduce the number of replicates required for each time interval, while producing results representative of exposure to residues on the pet for the pet hug exposure scenario. The study director will determine at what number of simulations that loading occurs and the increase of replicate number becomes moot.

The pilot study (for use with the pet hug portion of the study only) will be conducted in the following manner. 5 beagle dogs will be treated with Gokilaht between the shoulder blades on Day 0. Each treated dog will then be sampled using a different number of petting simulations at 24 hours post-application (HED has considered how each petting simulation will be performed, this is addressed in Changes to Parts B and C). The number of petting simulations (replicates) for each treated dog will be performed for either 1 simulation, 5 simulations, 10 simulations, 15 simulations, and 20 simulations (i.e., Dog #1 will have 1 simulations performed, Dog #2 will have 5 simulations performed, etc.). 2 pre-washed cotton gloves will be worn over a 5-mil Nitrile glove. All gloves will be analyzed separately and combined for each simulation to determine the appropriate number of replicates for the experimental study. Samples will be stored and shipped in glass containers. In addition, the study director will determine if breakthrough is occurring to the Nitrile glove. The Nitrile glove will only be required to be analyzed in the experimental study if breakthrough is occurring; however, whether occurring or not, it is necessary for test participants to continue to wear the Nitrile glove under the cotton layers.

HED is requiring some changes to the experimental study, as well as the addition of the pilot study, as addressed in Part A. General, 8. Experimental Summary. It was determined that the experimental study will be divided into two portions to better analyze the exposures representative of the pet hug and the hand-to-mouth scenarios. In addition, HED determined that the sampling of multiple time periods would be beneficial for analysis of Gokilaht activity on the treated pet for the pet hug portion of the experimental study. The updated sampling time periods are as follows: prior to application, 1, 6, and 24 hours after dosing, and on Days 2, 4, 7, 14, and 28 after dosing. The pet hug experimental study will be performed using the number of simulations (replicates) which

were determined appropriate from the pilot study for the updated sampling time periods. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of glove analysis. All other variables of the test system will remain the same.

The hand-to-mouth portion of the experimental study will be conducted as follows. HED determined that a 1 simulation set repeated for 10 dogs, prior to and 24 hours after application, will be acceptable for representation of this exposure scenario. The 10 dogs required for this sample set will be a separate group from those used in the pilot study, or the other portion of the experimental study. All other variables of the test system will remain the same.

Changes to Parts B. and C.

Most of the changes in Parts B. Experimental Design and C. Analysis of Sergeant's Pet Care, Inc. draft protocol are reflective of the alterations deemed necessary by HED and explained previously in Part. A. General. The following changes will be found in HED's reviewed protocol (only the sections that have changed are outlined below):

B. Experimental Design

1. Test System – Gloves

The draft protocol recommended cotton gloves only. HED recommends two pairs of cotton gloves with a 5 mil Nitrile glove underneath be worn for all study replicates.

2. Test System – Animals

d. Quantity

The draft protocol recommends the use of 10 beagle dogs for the proposed study. After review, HED recommends the use of 25 beagle dogs total for the entire study. This total includes 5 dogs for the pilot study, 10 dogs for the pet hug portion of the experimental study, and 10 dogs for the hand-to-mouth portion of the experimental study.

6. Post-Treatment Test Sampling

Changes recommended by HED for this section have been described in detail under Changes Made for Part A. General, # 9. Experimental Study (below). A description of how the petting simulation will be performed is included in HED's revised protocol. The petting simulation will be performed in the same manner for all parts (pilot, and experimental (pet hug, hand-to-mouth) studies) of the protocol. The description, as written in the revised protocol, is as follows:

The petting simulation or stroke will be performed in a manner which has been determined to mimic normal petting actions as well as actions that may occur during a child hugging the dog. Each stroke action will involve petting in a back-and-forth motion (2 pre-washed cotton gloves over 5 mil Nitrile glove) with splayed hands. The initial motion will be the back stroke, against the grain of the fur. This will be immediately followed by a forward motion, with the grain of the fur. These motions will be repeated starting with both sides (along the ribcage) of the dog, followed by the same motion along the back (dorsally). The two sides and back, in this order, with back-and-forth motion, will account for one stroke. This sequence of motions will be required for the pilot test and the experimental studies.

C. Analysis

2. Method of Analysis

The draft protocol describes cotton and latex glove collection for analysis. HED's revised protocol is changed to reflect analysis for two pairs of pre-washed cotton gloves and the 5 mil Nitrile glove (if breakthrough is determined from the pilot study).

Draft Protocol as Revised by HED for the Proposed Pet Spot-on Study

A. General

1. Study Title: Dislodgeability of Gokilaht from the Haircoat of Dogs Treated with a Spot-on Formulation

2. Purpose: To measure the dislodgeability of the test article from the haircoats of dogs treated with a spot-on formulation containing Gokilaht

3. Regulatory Compliance: This study will be conducted in compliance with US EPA Good Laboratory Practice Standards 40 CFR 160.

All procedures must be in compliance with Animal Welfare Act Regulations. All methods can be found in STILLMEADOW, Inc. Standard Operating Procedures (SOPs).

4. Quality Assurance: The Quality Assurance Unit (QAU) will review the protocol. The study information will be entered into the Master Schedule. The study will be inspected at least once during its progress. Further inspections may be scheduled as needed to ensure the integrity of the study. Any deviations from SOPs, the Protocol, or Good Laboratory Practice Standards will be immediately reported to the Study Director and Management. The report will be audited, and a statement prepared and signed which shall specify the dates inspections were made and findings reported to Management and the Study Director.

5. Test Article: Gokilaht. Test article identification will include the name, batch number, and purity. The Sponsor will also provide information regarding safety, stability, storage conditions, and disposal. The Sponsor assumes responsibility for purity, stability, identity, synthesis methods and location of documentation.

6. Proposed Schedule: Proposed start date: XX XXX 06
Proposed end date: XX XXX 06

7. Study Director: Mel Kaminsky

8. Pilot Study Summary: The experimental study (pet hug) will be preceded by a pilot study. The pilot study has been determined necessary in order to decide upon the loading capacity of the sampling media as it pertains to the number (replicates) of petting simulations required for each time interval tested. This should reduce the number of replicates required for each time interval, while producing results representative of exposure to residues on the pet. It will be the duty of the study director to determine what number of petting simulations is necessary to load the sampling media, or at which point increasing the number of replicates becomes moot.

   To determine the appropriate number of replicates, 5 beagle dogs will be treated topically with Gokilaht between the shoulders on Day 0. Each treated dog will then be sampled using a different number of petting simulations (replicates) at 24 hours post-application. The number of petting simulations (replicates) for each treated dog will be performed for either 1 simulation, 5 simulations, 10 simulations, 15 simulations, and 20 simulations

(i.e., Dog #1 will have 1 simulations performed, Dog #2 will have 5 simulations performed, etc.). 2 pre-washed cotton gloves will be worn over a 5-mil Nitrile glove. All gloves will be analyzed separately and combined for each simulation to determine the appropriate number of replicates for the experimental study. Samples will be stored and shipped in glass containers. The study director will determine if breakthrough is occurring to the Nitrile glove. The Nitrile glove will only be required to be analyzed in the experimental study if breakthrough is occurring; however, whether occurring or not, it is necessary for test participants to continue to wear the Nitrile glove under the 2 cotton layers.

9. Experimental Study

Summary: The experimental study will consist of two separate portions, pet hug and hand-to-mouth. The pet hug experimental study will be performed using the number of simulations (replicates) which were determined appropriate from the pilot study. Using this number of simulations, 10 beagle dogs will be treated topically between the shoulder blades on Day 0. The dogs' coats will be stroked for the number of replicates determined by the pilot study for the following time periods: prior to application, 1, 6, and 24 hours after dosing, and on Days 2, 4, 7, 14, and 28 after dosing. A separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of all glove samples for a given time period (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

The hand-to-mouth portion of the experimental study will be conducted as follows. A set of 1 petting simulation replicates will be repeated for 10 dogs, prior to and 24 hours after application. The 10 dogs required for this sample set will be a separate group from those used in the pilot study, or the other portion of the experimental study. Like the pet hug portion of the experimental study, a separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of all glove samples for a given time period (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

10. Protocol Amendments: Any change or alteration in the protocol must be justified and approved by the Study Director and recorded in writing.

11. Sponsor

Audits: The Sponsor may send an authorized representative to inspect the test system and/ or data on STILLMEADOW, Inc. premises during normal working hours.

B. Experimental Design

1. Test System – Gloves	2 cotton gloves (pre-washed and verified for no impurities) with 5 mil Nitrile glove underneath
2. Test System – Animals	
a. Species:	Dogs
b. Strain/ Source:	Beagles or Mongrels; STILLMEADOW, Inc. dog colony
c. Species Justification:	The dog is the species requested by the sponsor.
d. Quantity:	25 Dogs (5 pilot study, and 20 experimental studies (10 – pet hug, 10 hand-to-mouth))
e. Age and Weight:	At least 6 months old when dosing is initiated. Weights will be approximately equal so that all dogs fall into one dosing range.
f. Identification:	Tattoos and cage cards
g. Health Status:	Normal growth, appearance, and behavior will be factors to select healthy animals for testing.
3. Animal Husbandry	
a. Cage:	Stainless steel, suspended, wire bottom cage; at least 3' x 4', or 3.5' x 5' kennel
b. Housing:	Individual
c. Food:	PMI 5L18 High Density Canine Diet or other commercial product

d. Water: Tap water; available ad libitum; water dish or automatic watering system. Municipal water supply analyzed by Texas Commission on Environmental Quality.

e. Contaminants: There are no known contaminants in the feed or water available to laboratory animals that would be expected to interfere with this study.

f. Environment: Environmental controls for the animal rooms will be set to maintain a temperature of approximately 22° ± 3°C, a relative humidity range of ~ 30 – 80%, a 12-hour light/dark cycle (regulated automatically), and room ventilation of approximately 10 – 12 air changes per hour.

4. Pretest:

a. Acclimation Period: Animals will be acclimated for a period of at least 5 days.

b. Pretest Body Weights and Observations: Animals will be weighed during the acclimation period. In-life observations will be conducted daily beginning on Day 3.

c. Pre-treatment Control Sampling: The dogs will serve as their own baseline controls by the taking of negative control samples prior to dosing. All sampling (control and test) will be done according to the stroking procedures described in Section B.6, Post-Treatment Test Sampling. There will be no continuous contemporaneous controls.

5. Test Article Administration:

a. Method of Administration: On Test Day 0, the dogs will be treated with their respective dose volume of the test formulation by administering the proper amount of the formulation from a syringe (without needle attached) as a spot or stripe to the skin on the dog's back. The dog's hair coat in the

treatment area will first be parted (using the tip of the syringe to part the dog's hair) and the dose will be applied per label instructions.

b. Justification for Method of Administration: Proposed method of treatment.

c. Dosing: Dogs will be dosed based on weight ranges indicated on the product label. Dogs weighing between 15 and 33 lbs (6.8 and 15 kg) will receive 1.5 mL as a spot or stripes to the dogs back between the shoulder blades. Dogs weighing between 33 and 66 lbs (15 to 30 kg) will receive 3.0 mL applied as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.

6. Post-treatment Test Sampling: The pilot test will be performed to determine the appropriate number of replicates for the experimental study. 5 beagle dogs will be treated topically between the shoulders on Day 0, and each will be sampled using a different number of petting simulations (replicates) at 24 hours post-application. The number of petting simulations (replicates) for each treated dog will be performed for either 1 stroke, 5 strokes, 10 strokes, 15 strokes, and 20 strokes. Pre-washed cotton gloves will be worn over 5 mil Nitrile gloves for all sampling petting simulations. Each glove (cotton and Nitrile (if determined necessary)) will be analyzed separately and combined to determine the appropriate number of replicates for the experimental study.

The petting simulation or stroke will be performed in a manner which was been determined to mimic normal petting actions as well as actions that may occur during a child hugging the dog. Each stroke action will involve petting in a back-and-forth motion (cotton gloves over 5 mil Nitrile glove) with splayed hands. The initial motion will be the back stroke, against the grain of the fur. This will be immediately followed by a forward motion, with the grain of the fur. These motions will be repeated starting with both sides (along the ribcage) of the dog, followed by the same motion along the back (dorsally). The two sides and back, in this order, with back-and-forth motion, will

account for one stroke. This sequence of motions will be required for the pilot test and the experimental studies.

The pet hug experimental study will be performed using the number of simulations (replicates) which were determined appropriate from the pilot study. Using this number of simulations, 10 beagle dogs will be treated topically between the shoulder blades on Day 0. The dogs' coats will be stroked for the number of replicates determined by the pilot study for the following time periods: prior to application, 1, 6, and 24 hours after dosing, and on Days 2, 4, 7, 14, and 28 after dosing. A separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of glove (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

The hand-to-mouth portion of the experimental study will be conducted as a set of 1 petting simulation replicates. This will be repeated for 10 dogs, prior to and 24 hours after application. The 10 dogs required for this sample set will be a separate group from those used in the pilot study, or the other portion of the experimental study. Like the pet hug portion of the experimental study, a separate glove will be used for each sampling event. Sampling may be discontinued if and when 2 non-detect samples are identified from the results of glove (cotton and Nitrile (if determined necessary)) analysis. All gloves will be analyzed using the method developed by the facility.

7. Test Article Accountability:

A comprehensive inventory of test substances received and used will be kept. The test article container(s) will be weighed and/or counted when received at the facility, and a record of all test articles used will be maintained.

8. Safety Precautions:

General safety precautions as required by laboratory SOPs will be followed. A 5 mil Nitrile glove will be worn under 2 cotton gloves to ensure the safety of the technician from any dislodged test substance that might soak through the cotton gloves. The Sponsor will supply basic toxicity data on the test article to be used. However, since the toxicity of the test article is not often well characterized, the laboratory

should be conservative in setting safety procedures. The Sponsor or Sponsor's Representative shall be notified of any personnel exposures requiring a physician's examination or care.

C. Analysis

1. Transfer of Material: Each glove used in the pilot and experimental studies (pre- and post-dose sampling) will be immediately placed in a separate container and hand delivered to the laboratory to be analyzed for residue. A sample tracking form detailing animal numbers, samples, date and time will accompany each sample delivered to the chemistry department. The results of the analyses and date/time analyzed will be included in the final report.

2. Method of Analysis: All gloves (cotton and Nitrile (if determined necessary)), including those used for stroking the animals and gloves used for field fortifications will be analyzed by using the test method developed and validated by the testing facility. The methods used for extraction and analysis will be documented in the data and the final report.

3. Reference Standards: For characterization of the active ingredient in the test article, certified active ingredient will be used as the analytical reference standard.

D. Data Management

1. Records: The following records will be maintained during the study and transferred to the laboratory archives upon study termination:

a. Protocol and protocol amendments (if any)
b. Final report and amendments (if any)
c. Study correspondence
d. Animal and glove receipt data
e. Test article receipt, identification as supplied by Sponsor, preparation, administration, and disposition
f. Test animal information: number, sex, source, strain, and age and glove identification information
g. Pretest body weights
h. General clinical signs

i. Other pertinent data

2. Data Storage — All raw data, the protocol, analytical data and final report will be retained at the laboratory in the archives.

3. Data Reporting — The final report will include:

a. Statement from the Quality Assurance Unit
b. Signature of the Study Director
c. A GLP Compliance Statement signed by the Study Director
d. Names of scientific personnel involved in the study
e. Dates of study initiation and termination
f. Identification, description, preparation, and storage of the test article
g. All pertinent animal data, animal husbandry, dosing information, and observation methods as well as glove information
h. Description of the dosing and sampling procedures
i. Body weights
j. General clinical signs
k. Results of glove analysis
l. The protocol as appendix

4. Report Submission: A final report will be submitted after termination of the analytical portion of the study.

EPA Seminar 6/22/06 2:00-3:00

Jim Messina	Exponent	202-772-4932
Mary Nauvel	Nauvel Inc. (Sergeants)	972-312-0083
Bob Scharf	Sergeant's	(402)938-7039
George LaRocca	EPA/RD/IB	703-620-8050
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6-15-06

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June 12, 2006

George LaRocca
Product Manager 13
Registration Division
U.S. Environmental Protection Agency
Office of Pesticide Programs
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Subject: Meeting Request
Project No. WD00758.000

Dear Mr. LaRocca:

On behalf of our client Sergeant's Pet Care Products, Inc. (2637 South 158th Plaza, Suite 100, Omaha, Nebraska 68130-1703, EPA Company Number 2517), Exponent is submitting a request to meet with appropriate EPA staff to discuss additional information to upgrade to acceptable three Etofenprox studies (MRID #46082302, MRID #45869402, and MRID #45869401). Additionally, Exponent wants to discuss the conduct of a new dislodgeability study in dogs with cyphenothrin. Finally, Exponent wants to discuss the pending cyphenothrin registrations. Please find enclosed a meeting agenda, information to upgrade the three etofenprox studies, and a draft protocol for the new dislodgeability study.

Exponent proposes meeting with you and other appropriate EPA staff for one-hour on one of the following days: June 21, 2006 or June 22, 2006. Please let us know what day and time is most convenient for EPA.

Please note that the enclosed information includes information claimed as *CONFIDENTIAL BUSINESS INFORMATION* (CBI). This information is marked as CBI and should not be released to any third party.

We appreciate the Agency's continued efforts on this project. If you have any questions, please contact me at (202) 772-4932.

Sincerely,

James Messina
Authorized Representative of
Sergeant's Pet Care Products, Inc.

Enclosures (2)

cc: Bob Scharf, Sergeant's
Larry Nouvel, Nouvel & Associates
Rick Tinsworth, Exponent

Exponent

Exponent
1730 Rhode Island Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

Sergeant's Pet Care Products
EPA Meeting Agenda
June 21 or 22, 2006

I. Introductions

II. Sergeant's Pet Care Products, Inc. Etofenprox Studies and Cyphenothrin registration actions

III. Discuss information to upgrade Etofenprox studies
   a. See attached information to upgrade the following studies:
      i. MRID 46082302
      ii. MRID 45869402
      iii. MRID 45869401

IV. Discuss the conduct of a new dislodgeability study
   a. See attached draft protocol
      i. Cyphenothrin
      ii. Dog

V. Discuss Pending Cyphenothrin Registrations
   a. 2517-IN
   b. 2517-IL
   c. 2517-ON

Pages 238-272*Claimed confidential by submitter*

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Sergeant's Pet Care Products
EPA Meeting Agenda
June 21 or 22, 2006

I. Introductions

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      i. Cyphenothrin
      ii. Dog

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   a. 2517-IN
   b. 2517-IL
   c. 2517-ON

G. LAROCCA
3/20/06

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March 17, 2006

George LaRocca
Product Manager 13
Registration Division
U.S. Environmental Protection Agency
Office of Pesticide Programs
Document Processing Desk
1801 South Bell Street
Room 266A, Crystal Mall 2
Arlington, VA 22202

Subject: March 9, 2006 Meeting Minutes
Project No. WD00758.000

Dear Mr. LaRocca:

On behalf of our client Sergeant's Pet Care Products, Inc. (2637 South 158th Plaza, Suite 100, Omaha, Nebraska 68130-1703, EPA Company Number 2517), Exponent is submitting meeting minutes from our March 9, 2006 meeting with the Agency.

If you have any questions, please contact me at (202) 772-4932.

Sincerely,

James Messina
Authorized Representative of
Sergeant's Pet Care Products, Inc.

Enclosures (1)

cc: Linda Deluise, EPA
Marion Johnson, EPA
Christina Swartz, EPA
Wade Britton, EPA
Karlyn Bailey, EPA
Lois Rossi, EPA
Bob Scharf, Sergeant's
Larry Nouvel, Nouvel & Associates
Rick Tinsworth, Exponent

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Sergeant's/EPA Meeting Minutes
March 9, 2006
10:00 A.M.

Attendees:

Name	Organization	Phone Number
Linda DeLuise	EPA/RD	703-305-5428
Wade Britton	EPA/RD/IB	703-305-5428
Marion J. Johnson, Jr.	EPA/RD/IB	703-305-6788
Karlyn Bailey	EPA/HED/RAB2	703-308-0004
Christina Swartz	EPA/HED/RAB2	703-305-5877
Lois Rossi	EPA/RD	703-305-5477
Larry Nouvel	Nouvel Inc./Sergeant's	469-233-2854
Alan Brown	Sergeant's/Sowell & Co.	214-871-3320
Bob Scharf	Sergeant's	402-938-7039
Jim Messina	Exponent	202-772-4932
Rick Tinsworth	Exponent	202-772-4912

The meeting was opened with introductions and a sign-in sheet was passed around. Alan Brown and Bob Scharf gave a general overview of Sergeant's Pet Care Products, Inc. and the importance of the pending cyphenothrin spot-on products to their business. They discussed the missed 2006 market and the direct effects on their business. These effects include a loss of credibility in the marketplace, loss of revenue for cyphenothrin and other products of theirs, complete loss of business with a major retailer in the Midwest that decided to drop Sergeant's products because they could not introduce the new cyphenothrin line of products.

Rick Tinsworth then addressed registration issues. Rick explained that Sergeant's met with EPA during 2001 to discuss the dislodgeability study design. At that time, there was not any approved protocol for the conduct of these type of studies. The Agency gave feedback to Sergeant's, although a protocol was not submitted to EPA for review. Additionally, during 2004 the EPA offered guidance on the risk assessment prepared and submitted by Sergeant's. The EPA suggested we use the carbaryl RED approach for the risk assessment. This approach was used in the risk assessment submitted to EPA. Recently, Exponent spoke with Jeff Evans of HED, who stated that the source of the method for the recent EPA spot-on postapplication exposure assessment is SOP 13: Postapplication Exposure Assessment for Children from Pet Treatments. Our understanding is that this SOP is not final but Mr. Evans did provide notes from the ExpoSac meeting (January 10, 2002), at which the policy was discussed. These notes state, "The products that are used to control pests on animals are varied and can include

dusts, dips and shampoos, collars, spot-ons, and feed-throughs. The Agency is interested in the use of any of these that results in exposure to children although the Agency generally is not concerned about feed-throughs and spot-ons based on how they are used."

Mr. Tinsworth also discussed the assumption used in EPA's risk assessment of stroking the pet 20 times in 2 hours during a 24-hour period. He stated that this seems like an overestimate to us.

Based on these issues and Sergeant's efforts to develop data and prepare a risk assessment based on EPA guidance, we would like the Agency to consider a conditional registration with the requirement to conduct a new product specific dislodgeability study on dogs. We would want the EPA to review and approve the protocol for this type of study, so that all are in agreement on how it is conducted.

Mr. Tinsworth then stated that there are big differences between the etofenprox dislodgeability studies and the tetrachlorvinphos study that the EPA used. Sergeant's studies are on a pyrethroid, spot-on use, gel product, whereas the tetrachlorvinphos study is an organophosphate, spray product, liquid. We believe that these differences are major and that the Agency should use the etofenprox studies for the risk assessment. Additionally, the EPA granted etofenprox registrations to Sergeant's and a recent (January 2006) etofenprox registration to Wellmark International. If the Sergeant's studies were not sufficient to be used for risk assessment purposes for cyphenothrin, we asked what did the EPA use for etofenprox. If the EPA used the Sergeant's studies to support etofenprox then we believe they should also use them to support cyphenothrin.

Mr. Tinsworth then discussed the comparison table of EPA's risk assessment approach, Exponent's original risk assessment approach (based on Carbaryl RED), and a revised risk assessment approach based on January 2002 ExpoSac notes. We stated that based on the summary table the only big difference is the transferable fraction that was used. The EPA used 5% and Exponent used 0.05% from the 2002 etofenprox dislodgeability study. Mr. Tinsworth suggested that the EPA could use a transferable fraction of 0.5% to allow for possible errors in the Sergeant's study and the MOE's still would be acceptable.

Ms. Swartz stated that the Wellmark International risk assessment was based on EPA defaults and that the Agency did not need to rely upon the Sergeant's studies. She said that she would look into this and other etofenprox registrations to confirm.

Ms. Swartz then stated that the quality of the studies submitted by Sergeant's is in question. The main issue is that Sergeant's used latex gloves instead of the standard cotton gloves. Other issues include: LOQ and fortification tables were not provided, extraction procedures were not provided, recoveries were low (47-54%), and HPLC information was not provided. Sergeant's explained that a method validation study was submitted to EPA with the studies. The MRID is 45869402. The EPA stated they did not review the validation study. A copy of the study was provided during the meeting. The EPA agreed to review the study and get back to us. Additionally, Sergeant's

explained that out of the two studies submitted, we did not use the study with non-detects. Instead we used the original study with residues up to 0.05%. Sergeant's also explained that latex gloves were used because higher recoveries were obtained as compared to using cotton. This information is also included in the validation study.

The Agency stated they would look into the guidance to use the Carbaryl RED, they will review the validation study, and they will look at the toxicology endpoint information. They Agency agreed to have an internal meeting once they complete the above work.

Mr. Tinsworth emphasized that the registrations are important and that if the Agency can look into them and grant them (even if they were conditional), we would appreciate it.

Sergeant's thanked EPA for taking the time to meet with them and then the meeting was adjourned.

Christina Swartz/DC/USEPA/US
03/10/2006 05:17 PM

To: Lois Rossi/DC/USEPA/US@EPA, George LaRocca/DC/USEPA/US@EPA, Marion Johnson/DC/USEPA/US@EPA
cc: Wade Britton/DC/USEPA/US@EPA, Karlyn-J Bailey/DC/USEPA/US@EPA
bcc:
Subject: cyphenothrin

Lois, George, Marion,
Just wanted to update you on the status of the etofenprox study reviews (Sergeant's/Exponent wanted to use these studies to support their product w/cyphenothrin).

The review of the first study has been completed/posted to the database. Wade is in the process of reviewing the second study, and should be able to complete it shortly, and after I send him a bean. The glove validation study they brought to the meeting has just been reviewed by RAB3, and we did not agree that it could be used to render the other study (or the one Wade is reviewing) acceptable. Jack Arthur remembers discussing the study design with the registrant, but is not aware that a protocol was actually submitted as a follow-up. I spoke with him briefly yesterday, and he said that for the etofenprox review, they went with the 5% transfer, also based on the TCVP study that Wade cited in his review.

Bob Scharf e-mailed me a table today comparing application rates, and they are similar to or lower than others on the market when normalized to the weight of the dog, so my understanding that their application rates were higher is incorrect. Wade concurred with what Bob sent me.

The other follow-up note I have is to touch base with Jeff Evans (when he gets back) regarding what about the carbaryl RA would be relevant for cyphenothrin.

I've attached the reviews that are available so far.

Yours,
Christina


D298228a.mem.wpd

D298228.mem.wpd

Christina Swartz
US EPA, Office of Pesticide Programs
Health Effects Division
Phone: 703 305 5877
Fax: 703 305 5147

e-mail: Swartz.Christina@epa.gov

Sergeant's/EPA
Meeting Agenda
Proposed Meeting Dates/Times
March 9, 2006
10:00 AM

I. Introductions

II. Sergeant's Company Update
   a. Urgency of resolving issues and obtaining registrations
      i. Loss of customers and revenue
      ii. Damage to reputation in marketplace

III. Cyphenothrin Spot-On for Dogs
   a. EPA File Symbol 2517-IN and 25617-IL
   b. Use of use-specific and chemical class-specific dislodgeability data (MRID 45869401 and 46082302)
      i. EPA reviews
      ii. EPA issues

IV. Cyphenothrin + IGR Squeeze-On for Dogs
   a. EPA File Symbol 2517-IN
   b. Use of use-specific and chemical class-specific dislodgeability data (MRID 45869401 and 46082302)
      i. EPA reviews
      ii. EPA issues

V. Cyphenothrin + Methoprene Squeeze-On for Dogs
   a. EPA File Symbol 2517-ON
   b. Use of use-specific and chemical class-specific dislodgeability data (MRID 45869401 and 46082302)
      i. EPA reviews
      ii. EPA issues

VI. Conclusions

Table 1. Comparison of Exposure and Risk Assessment Approaches for Cyphenothrin Spot-On Product

	EPA SOP – tetrachlorvinphos spray-on study (EPA Jan 2002 ExpoSac notes)	**EPA SOP – etofenprox spot-on study** (EPA Jan 2002 ExpoSac notes)	**Exponent approach in 2004 cyphenothrin assessment** (based on EPA 2003 carbaryl RED)
Dermal Postapplication Exposure for Cyphenothrin Spot-on Products (Day of Treatment)			
Standard dog size	30 lb; 5986 cm^2	30 lb; 5986 cm^2	30 lb; 6000 cm^2
Amount applied	645 mg	645 mg	645 mg
Hug surface area	1875 cm^2	1875 cm^2	Not applicable
Transferable fraction	5% (dislodgeable fraction from tetrachlorvinphos pump-spray)	0.05% (fraction of applied etofenprox spot-on removed on day of treatment)	0.05% (fraction of applied etofenprox spot-on removed on day of treatment)
Dermal absorption	20%	20%	20%
Body weight	15 kg	15 kg	15 kg
Exposure calculation	(645 mg × 5%)/5986 cm^2 × 1875 cm^2 × 20% / 15 kg = 0.135 mg/kg/d	(645 mg × 0.05%)/5986 cm^2 × 1875 cm^2 × 20% / 15 kg = 0.00135 mg/kg/d	645 mg × 0.05% × 20% / 15 kg = 0.0043 mg/kg/d
MOE (NOAEL = 10 mg/kg/d)	74	7,400	2,300
Oral Postapplication Exposure for Cyphenothrin Spot-on Products (Day of Treatment)			
Standard dog size	30 lb; 5986 cm^2	30 lb; 5986 cm^2	30 lb; 6000 cm^2
Amount applied	645 mg	645 mg	645 mg
Transferable fraction	5% (dislodgeable fraction from tetrachlorvinphos pump-spray)	0.05% (fraction of applied etofenprox spot-on removed on day of treatment)	0.05% (fraction of applied etofenprox spot-on removed on day of treatment)
Contact area	20 cm^2/event	20 cm^2/event	20 cm^2/event
Contact frequency	20 events/hr	20 events/hr	1 event/day
Exposure duration	2 hr/day	2 hr/day	Not applicable
Saliva extraction	50%	50%	50%
Exposure calculation	(645 mg × 5%)/5986 cm^2 × 20 cm^2/cv × 20 ev/hr × 2 hr/d × 50% / 15 kg = 0.144 mg/kg/d	(645 mg × 0.05%)/5986 cm^2 × 20 cm^2/ev × 20 ev/hr × 2 hr/d × 50% / 15 kg = 0.00144 mg/kg/d	(645 mg × 0.05%)/6000 cm^2 × 20 cm^2/ev × 1 ev/d × 50% / 15 kg = 0.0000358 mg/kg/d
MOE (NOAEL = 10 mg/kg/d)	70	7,000	279,000
Total MOE	36	3,600	2,300

PART 1. COMPARISON OF 2002 AND 2003 ETOFENPROX POST-TREATMENT STUDIES

	2002 Study	2003 Study
Number of cats	8 cats	8 cats
Weight of cats	1.5 – 6.4 kg	2.0 – 4.8 kg
Doses	4 groups, based on animal weight: • 0.4 mL (237.7 mg) • 0.8 mL (475.5 mg) • 1.2 mL (713.2 mg) • 2.75 mL (1634.4 mg)	2 groups (<2.6 kg, >4.6 kg) at dose rate of 330 mg/kg BW: • 1.1-1.4 mL (~700 mg) • 2.6-2.7 mL (~1480 mg)
Conclusion	Low level residues detected on gloves detected at 4 hours post-treatment (0.12 – 0.27 mg) and 24 hours post-treatment (<0.12 – 0.15 mg). Using adjusted residue data (1.89X), the percent dislodgeable is 0.05% at 4 hours and 0.03% at 24 hours for the two middle dose groups (i.e., those that bracket cyphenothrin dose rate). Non-detectable residues (<0.12 mg) were found at all other sampling times (3 days, 7 days, 22 days, 28 days)	No detected residues on gloves at 4 hours, 24 hours or 48 hours after dosing. The LOD seems to be 0.12 mg (although this should be confirmed). At ½ LOD, using adjusted data (1.97X) the maximum percent dislodgeable would be estimated as 1.97 × 0.06 mg / 616 mg = 0.02%.

The data from these studies are essentially consistent. The 2002 data, which indicate low detectable levels at 4 and 24 hours post-treatment, result in the more conservative estimate of exposure. A further advantage of the 2002 study is that sampling was conducted up to 28 days post-treatment, which allows estimation of exposure over the "long-term".

In conclusion, the **maximum** percent dislodgeable observed in these two studies is 0.05% at 4 hours post-treatment.

Pages 282-283*Claimed confidential by submitter*

Sergeant's/EPA
Meeting Agenda
Proposed Meeting Dates/Times
March 1, 2, 3, 2006
Morning Meeting

I. Introductions

II. Sergeant's Company Update
   a. Urgency of resolving issues and obtaining registrations
      i. Loss of customers and revenue
      ii. Damage to reputation in marketplace

III. Cyphenothrin Spot-On for Dogs
   a. EPA File Symbol 2517-IN and 25617-IL
   b. Use of use-specific and chemical class-specific dislodgeability data (MRID 45869401 and 46082302)
      i. EPA reviews
      ii. EPA issues

IV. Cyphenothrin + IGR Squeeze-On for Dogs
   a. EPA File Symbol 2517-IN
   b. Use of use-specific and chemical class-specific dislodgeability data (MRID 45869401 and 46082302)
      i. EPA reviews
      ii. EPA issues

V. Cyphenothrin + Methoprene Squeeze-On for Dogs
   a. EPA File Symbol 2517-ON
   b. Use of use-specific and chemical class-specific dislodgeability data (MRID 45869401 and 46082302)
      i. EPA reviews
      ii. EPA issues

VI. Conclusions

Marion Johnson/DC/USEPA/US
02/09/2006 02:16 PM

To George LaRocca/DC/USEPA/US@EPA
cc
bcc
Subject Fw: cyphenothrin risk assessment

FYI !!!!

Marion J. Johnson, Jr.,
Chief, Insecticide Branch
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
(703) 305-6788 (tel.)
(703) 305-6596 (fax)
johnson.marion@epa.gov
visit: http://www.epa.gov/pesticides

----- Forwarded by Marion Johnson/DC/USEPA/US on 02/09/2006 02:14 PM -----

Christina Swartz/DC/USEPA/US
02/03/2006 05:23 PM

To Lois Rossi/DC/USEPA/US@EPA, Marion Johnson/DC/USEPA/US@EPA
cc Wade Britton/DC/USEPA/US@EPA, Catherine Eiden/DC/USEPA/US@EPA
Subject cyphenothrin risk assessment

Lois, et. al.,
Please see the attached risk assessment document prepared by Wade, for the proposed use of cyphenothrin on pets. The RA also includes the existing uses. As a point of clarification (and as I discussed with you Lois), the target MOE here is shown to be 100 for all scenarios, but would be 1000 for adult handlers (due to the lack of an acceptable developmental toxicity study). Since adult handler MOEs were all much greater than 1000, the conclusions of the memo don't change. RAB2 would like to prepare an additional document that includes the executive summaries of the toxicity studies that were reviewed, including the 2 unacceptable developmental toxicity studies. We will be happy to provide additional guidance on what additional data (e.g., potentially a dermal toxicity study) or other options (such as lowering the application rate) might be used to alleviate the risk concerns for postapplication exposure to toddlers.

Please let me know if you need more information.

Yours,
Christina

D317077MEM.doc

Christina Swartz
US EPA, Office of Pesticide Programs
Health Effects Division
Phone: 703 305 5877
Fax: 703 305 5147

e-mail: Swartz.Christina@epa.gov

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: November 30, 2004

MEMORANDUM

Subject: EPA File Symbol: 2517-IL SERGEANT'S CYPHENOTHRIN SQUEEZE-ON FOR DOGS
DP Barcode: D305953
Decision No.: 345654
PC Code: 129013 Cyphenothrin (CAS #39515-40-7)

From: Byron T. Backus, Ph.D.
Technical Review Branch
Registration Division (7505C)

Byron T. Backus 11/30/2004

To: Linda DeLuise/George LaRocca RM 13
Insecticide Branch
Registration Division (7505C)

Applicant: SERGEANT'S PET CARE PRODUCTS, INC.

FORMULATION DECLARATION FROM LABEL:

Active Ingredient(s):	% by wt
Cyphenothrin (CAS #39515-40-7)	40.0%
Inert Ingredients:	60.0%
Total:	100.00%

ACTION REQUESTED:

The Risk Manager requests:

> Waiver request [for] acute inhalation; refer to 2517-IN for other studies and companion animal [study].

BACKGROUND:

The data cited and previously reviewed (for EPA File Symbol 2517-IN) includes an acute oral LD_{50} study (rat, up-and-down procedure, defaulting to an acute toxic class procedure, MRID 46166103); acute dermal LD_{50} study (rat; MRID 46166104); primary eye irritation study (rabbit; MRID 46166105); primary dermal irritation study (rabbit; 46166106) and a dermal sensitization study (guinea pig; 46166107), as well as a companion animal safety study in dogs (MRID 46166108). The five acute toxicity studies were conducted at Product Safety Labs, New Jersey. The companion animal safety study was conducted at Stillmeadow, Inc. In addition, there is a waiver request for an inhalation study. All studies were conducted on Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL, containing 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar.

RECOMMENDATIONS:

1. The companion animal (dog) safety study in MRID 46166108 has been reviewed and has been classified as acceptable for puppies (12 weeks and older) and adult dogs. It is concluded that there is an adequate margin of safety (at least 5X) between the exposure associated with the proposed use level for this formulation in dogs, and that at which significant adverse systemic effects (not seen in this study, but which might include ear twitching, muscle tremors, drooling) may occur. For dermal effects an effect was observed in one puppy in Group III (treated at essentially a 7.5X dose level), but in none of the other dogs (including the puppies in Group II, dosed at 1.5X) indicating a reasonably low potential for this effect in dogs treated at the proposed use level.

2. It is noted that the test material in the companion animal (dog) safety study was supplied in (and applied from) unidose 1.5 mL ampules. However, the report states that the mean volume delivered from a single 1.5 mL ampule was 1.17 mL, and the registrant is proposing packaging this product in 3.0 and 4.5 (as well as 1.0 and 1.5) mL tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2 x 1.17) mL and the 4.5 mL tubes deliver no more than 3.51 (3 x 1.17) mL.

3. The five acute toxicity studies have been reviewed and classified as acceptable. In addition, TRB has no objection to the registrant's waiver request for an acute

inhalation study, based on the product form (a liquid), its proposed packaging (1.0, 1.5, 3.0 or 4.5 mL tubes or ampules), the method of application (as a spot-on or stripe-on to the dog's back), and the relatively low inhalation toxicity of technical Cyphenothrin (one report from the open literature gives a rat LC50 of 1.85 mg/L, or EPA toxicity category III; extrapolating from this the inhalation LC50 value for a 40% Cyphenothrin-60% inert product would then be greater than 4 mg/L, or EPA toxicity category IV by this exposure route).

4. Based on the results of the acute toxicity studies, the following is the acute toxicity profile for EPA File Symbol: 2517-IL SERGEANT'S CYPHENOTHRIN SQUEEZE-ON FOR DOGS. The signal word of the product would be CAUTION, as proposed by the registrant:

Study Type	Tox. Cat.	Classification & MRID #
Acute Oral LD_{50} (rat)	III	Acceptable (#46166103)
Acute Dermal LD_{50} (rat)	III	Acceptable (#46166104)
Acute Inhalation LC_{50}	IV	Waived
Primary Eye Irritation (rabbit)	III	Acceptable (#46166105)
Primary Dermal Irritation (rabbit)	IV	Acceptable (#46166106)
Dermal Sensitization (guinea pig)	Negative	Acceptable (#46166107)

5. Based on the acute toxicity profile and proposed uses, the following is the precautionary labeling for this product, as obtained from the Label Review System:

PRODUCT ID #: **002517-00085**

PRODUCT NAME: **SERGEANT'S CYPHENOTHRIN SQUEEZE-ON FOR DOGS**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **CAUTION**

Hazards to Humans and Domestic Animals:

Harmful if swallowed or absorbed through skin.. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical advice.

Reviewer: Byron T. Backus, Ph.D. **Date:** November t9, 2004
Risk Manager (EPA): t3

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.t100; OECD 425

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666 t03) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. t1 of MRID 46t66104 the specific gravity of the test material was t.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IL Sergeant's Cyphenothrin Squeeze-On for Dogs (although this product does not contain either Nylar or Methoprene) with a label declaration of: Cyphenothrin 40.0%.

CITATION: Moore, G. (2003) Acute Oral Toxicity Up and Down Procedure in Rats: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: t3320, P320/UDP. Unpublished study prepared by Product Safety Labs, Food Product Laboratory and Silliker Laboratories of New Jersey, Inc. 16 p. Study Completion Date: May 20, 2003. MRID 46t66103.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 88t0 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46166103), conducted using the up-and-down procedure but defaulting to the acute toxic class method, Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared, a clear, light yellow liquid with a specific gravity of 1.06t g/mL containing 39.87% Gokilaht (Cyphenothrin), 3.0% Methoprene and 2.00% Nylar was administered by oral gavage at 2000 mg/kg to a single Sprague-Dawley derived 9-week-old albino fasted (overnight) female rat. When this rat survived, four additional fasted (overnight) female rats of the same strain, age, body weight range (164-t82 g) and source (Ace Animals, Inc., Boyertown, PA) were also dosed at 2000 mg/kg.

On the day of dosage rats were observed for several hours for mortality and signs of gross toxicity for several hours post-dosing. They were then observed at least once a day for the remainder of the t4-day observation period.

On the day of dosage rats were observed at least 3 times within the first 4 hours after dosing for clinical signs of toxicity and mortality and then at least once daily for the remainder of the t4-day observation period. Individual body weights were recorded just prior to dosing (Day 0) and on days 7 and 14. Individual body weights were recorded predosing and on days 7 and 14.

Two rats died within 24 hours of dosage with no clinical signs observed prior to death. Two rats which survived showed reduced fecal volume, ventral staining and hypoactivity, with recovery by Day 4. All survivors gained weight in the period from Day 0 (predose) to Day 7 and again from Day 7 to 14.

Postmortem necropsy findings in the rats which died showed discoloration of the lungs and intestines and fluid filled stomachs. Gross necropsy findings in rats surviving to terminal sacrifice were unremarkable.

Estimated Oral LD_{50} in female rats > 2000 mg/kg.

EPA File Symbol 2517-IL Sergeant's Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA Toxicity Category III based on the results of testing of a liquid with a specific gravity of 1.061 g/mL containing 40% Cyphenothrin, 2% Pyriproxyfen (Nylar) and 3% Methoprene, based on the observed LD_{50} (>2000 mg/kg) in female rats.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 16), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Friday, October 15, 2004, 4:37:11 PM
Data file name: Cyphenothrin-IGR.dat
Last modified: 10/15/2004 4:37:11 PM

Test/Substance: Cyphenothrin-IGR
Test type: Limit Test
Limit dose (mg/kg): 2000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	8040	2000	O	O
2	8198	2000	O	O
3	8239	2000	O	O
4	8372	2000	X	X
5	9407	2000	X	X

(X = Died, O = Survived)

Dose Recommendation: The limit test is complete.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
2000	3	2	5
All Doses	3	2	5

Statistical Estimates:

The LD50 is greater than 2000 mg/kg.

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	-	2/5	-

Statistics - Not necessary to compute the oral LD_{50}.

A. Mortality - As noted in the table above.

B. Clinical observations - Two rats died within 24 hours of dosage with no clinical signs observed prior to death. Two rats which survived showed reduced fecal volume, ventral staining and hypoactivity, with recovery by Day 4. All survivors gained weight in the period from Day 0 (predose) to Day 7 and again from Day 7 to 14.

C. Gross Necropsy - Postmortem necropsy findings in the rats which died showed discoloration of the lungs and intestines and fluid filled stomachs. Gross necropsy findings in rats surviving to terminal sacrifice were unremarkable.

D. Reviewer's Conclusions: The study is acceptable. EPA File Symbol 2517-IL Sergeant's Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA toxicity category III for oral toxicity based on the results from testing a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 40% Cyphenothrin, 2% Pyriproxyfen (Nylar) and 3% Methoprene based on the observed LD_{50} (>2000 mg/kg) in female rats.

E. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 22, 2004
Risk Manager (EPA): 13

STUDY TYPE: Acute Dermal Toxicity - Wistar rats - OPPTS 870.1200; OECD 402

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IL Sergeant's Cyphenothrin Squeeze-On for Dogs (although this product does not contain either Nylar or Methoprene) with a label declaration of Cyphenothrin 40.0%.

CITATION: Moore, G. (2003) Acute Dermal Toxicity Study in Rats - Limit Test: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13321, P322. Unpublished study prepared by Product Safety Labs, Food Product Laboratory and Silliker Laboratories of New Jersey, Inc. 16 p. Study Completion Date: May 20, 2003. MRID 46166104.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID #46166104), a group (5M & 5F) of Sprague-Dawley derived albino rats (source: Ace Animals, Inc., Boyertown, PA; Males: 300-318 g; Females: 178-204 g; young adult [indicated by body weight data]) were dermally exposed (approximately 10% of body surface) for 24 hrs to 2000 mg/kg of undiluted Cyphenothrin-IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen). The test material was held in contact by a gauze pad and Durapore tape.

Rats were observed several times after application on day 0 and once daily thereafter for 14 days. Individual body weights were recorded just prior to dosing (day 0) and on days 7 and 14.

There was no mortality and there were no signs of systemic toxicity. Three males showed some dermal irritation (erythema and/or edema) with clearing by day 2. All rats gained weight from day 0 to 7 and from day 7 to 14.

No gross abnormalities were observed at post-sacrifice necropsy.

Dermal LD_{50} Males > 2000 mg/kg (0/5 died)
Females > 2000 mg/kg (0/5 died)
Combined > 2000 mg/kg (0/10 died)

Cyphenothrin-IGR Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA toxicity category III in terms of dermal toxicity based on the testing of Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared, a clear, light yellow liquid with a

specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar with a rat LD_{50} > 2000 mg/kg,

This acute dermal study is classified as acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 16), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Statistics - Not necessary to compute the dermal LD_{50}.

A. Mortality - None, as noted in the table above.

B. Clinical observations - There were no signs of systemic toxicity. Three males showed some dermal irritation (erythema and/or edema) with clearing by day 2. All rats gained weight from day 0 to 7 and from day 7 to 14.

C. Gross Necropsy - No gross abnormalities were observed at post-sacrifice necropsy.

D. Reviewer's Conclusions: The study is acceptable. Cyphenothrin-IGR Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA toxicity category III in terms of dermal toxicity based on the testing of Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared, a clear, light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar with a rat LD_{50} > 2000 mg/kg.

E. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 23, 2004
Risk Manager (EPA): 13

STUDY TYPE: Primary Eye Irritation - NZW Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IN Sergeant's Cyphenothrin Squeeze-On for Dogs (although this product does not contain Methoprene or Pyriproxyfen) with a label declaration of Cyphenothrin 40.0%.

CITATION: Moore, G. (2003) Primary Eye Irritation Study in Rabbits: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13322, P324. Unpublished study prepared by Product Safety Labs, Food Products Laboratory and Silliker Laboratories of New Jersey, Inc. 17 p. Study Completion Date: May 20, 2003. MRID 46166105.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46166105), 0.1 mL of undiluted Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen), was instilled into the conjunctival sac of one eye of each of 3 adult New Zealand White Rabbits (weights: not reported; ages: young adult; source: Davidson's Mill Farm, South Brunswick, NJ), with observations and scoring at 1, 24, 48 and 72 hours after instillation.

No corneal opacity was observed (with 2% ophthalmic fluorescein sodium used at 24 hours to verify the absence of corneal opacity at that reading). 3/3 eyes were positive for conjunctival redness (score of 2) at 1 and 24 hours. All eyes were completely clear (all scores zero) at 72 hours.

Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA toxicity category III for eye irritation, based on the findings (presence of grade 2 conjunctival redness in 3/3 eyes at 24 hrs with subsequent clearing by 72 hrs) from a study with Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen).

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 17), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested			
	1 hr	24 hrs[2]	48 hrs	72 hrs
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness[1]	3/3	3/3	0/3	0/3
Chemosis[1]	0/3	0/3	0/3	0/3
Discharge[1]	3/3	0/3	0/3	0/3

[1]Score of 2 or more considered positive
[2]Fluorescein staining was used to verify the absence of corneal opacity.

A. **Observations** - No systemic effects were observed. 3/3 eyes were positive for conjunctival redness (score of 2) at 1 and 24 hours. All eyes were completely clear (all scores zero) at 72 hours.

B. **Reviewer's Conclusions:** The study adequately defines a Toxicity Category III hazard potential in terms of eye exposure potential for Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) based on the findings of this study conducted on Cyphenothrin + IGR Squeeze-On for Dogs, a clear, light yellow liquid with a specific gravity of 1.06 t g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen).

C. **Deficiencies** - None

Reviewer: Byron T. Backus, Ph.D. **Date:** November 23, 2004
Risk Manager (EPA): 13

STUDY TYPE: Primary Dermal Irritation - NZW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IL Sergeant's Cyphenothrin Squeeze-On for Dogs (although this product does not contain Methoprene or Pyriproxyfen) with a label declaration of Cyphenothrin 40.0%.

CITATION: Moore, G. (2003) Primary Skin Irritation Study in Rabbits: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13323, P326. Unpublished study prepared by Product Safety Labs, Food Products Laboratory and Silliker Laboratories of New Jersey, Inc. 17 p. Study Completion Date: May 20, 2003. MRID 46166106.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46166106), 0.5 mL aliquots of undiluted Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen), were applied to dermal sites on each of 3 (2M & 1F) young adult New Zealand White albino rabbits (source: Davidson's Mill Farm, South Brunswick, NJ) with 4-hour semioccluded exposure.

After 4 hours, the gauze patch and holding tape were removed. The test sites were scored (Draize) at 1, 24, 48 and 72 hrs and at 7 and 10 days.

No edema was observed (all scores for edema were zero). All sites scored one for erythema at 1 hour and 2 at 24, 48 and 72 hours. One site scored 2 for erythema on day 7 while the other two scored 1. All scores were zero on day 10. The PII (average of scores at 1, 24, 48 & 72 hrs) = 1.75.

Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA Toxicity Category IV for dermal irritation effects, based on the findings (PII of 1.75 and relatively low score (grade 2, characterized as well-defined) for erythema at 72 hrs [EPA Toxicity Category III would be characterized by moderate or grade 3 erythema at 72 hrs] following 4-hr semi-occluded exposure) from a study conducted on Cyphenothrin + IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen).

This study is classified as acceptable. It does satisfy the guideline requirement for a primary

dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 17), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

A. Observations - No edema was observed (all scores for edema were zero). All sites scored one for erythema at 1 hour and 2 at 24, 48 and 72 hours. One site scored 2 for erythema on day 7 while the other two scored 1. All scores were zero on day 10. The PII (average of scores at 1, 24, 48 & 72 hrs) = 1.75.

B. Results - The PII (average of 1, 24, 48 and 72-hour scores) = 1.75 The mean irritation score on day 3 was 2.0 (erythema: 2.0; edema: 0.0).

C. Reviewer's Conclusions - Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) is in EPA Toxicity Category IV in terms of dermal irritation based on the results from testing with Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen).

D. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. Date: November 23, 2004
Product Manager (EPA): 13

STUDY TYPE: Dermal Sensitization - albino Guinea Pig; OPPTS 870.2600; OECD 406, 429

TEST MATERIAL (% a.i.): Cyphenothrin-IGR Squeeze-On for Dogs (2824) MGK GLP Project #1683A - Lab Prepared. From the certificate of analysis (p. 15 of MRID 4666103) this contained 39.87% Gokilaht (Cyphenothrin), 3.00% Methoprene and 2.00% Nylar. From information on p. 11 of MRID 46166104 the specific gravity of the test material was 1.061 g/mL. The test material is described as a clear, light yellow liquid.

SYNONYMS: The test material description is consistent with the proposed product 2517-IL Sergeant's Cyphenothrin Squeeze-On for Dogs (although this product does not contain Methoprene or Nylar) with a label declaration of Cyphenothrin 40.0%.

CITATION: Moore, G. (2003) Dermal Sensitization Study in Guinea Pigs: Buehler Method: Cyphenothrin-IGR Squeeze-On for Dogs. Project Number: 13324, P328. Unpublished study prepared by Product Safety Labs, Food Products Laboratory and Silliker Laboratories of New Jersey, Inc. 25 p. Study Completion Date: May 20, 2003. MRID 46166107.

SPONSOR: MCLAUGHLIN GORMLEY KING COMPANY, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46166107) with Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen), a group of 20M Hartley albino guinea pigs (373-428 g; young adult; source: Elm Hill Breeding Labs, Chelmsford, MA) were each dermally exposed (6 hours) to a 0.4 mL aliquot of test material on a once-a-week basis for 3 consecutive weeks. After a two week rest period they were then dermally challenged with 0.4 mL of a 75% w/w mixture of the test material in mineral oil at a previously unexposed site. An additional 10 previously unexposed male guinea pigs received were similarly treated. Challenge sites on all 30 guinea pigs were evaluated and scored for erythema at 24 and 48 hours after the application.

Following challenge, 7/20 previously exposed guinea pigs showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours. 4/10 controls showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours.

The report includes results from a positive control study (PSL Study #12371) which was conducted with technical (85%) alpha-Hexylcinnamaldehyde and completed on August 15, 2002. The results (3/10 previously exposed, 0/5 naive control guinea pigs showing a positive response at challenge) were appropriate. The study dates for the testing with Cyphenothrin-IGR Squeeze-On for Dogs were from March 13 to April 11, 2003. While slightly outside the 6-month period indicated in the Guidelines, it is concluded the overall study findings are acceptable.

In this study **there were no indications that Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is a dermal sensitizer.**

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (**OPPTS** 870.2600; OECD 406, 429) in the Guinea pig.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 25), and [No] Data Confidentiality (p. 2) statements were provided.

I. PROCEDURE

A. Induction - Each of 20 male Hartley albino guinea pigs was treated once a week for 3 consecutive weeks to a 6-hour exposure to 0.4 mL undiluted Cyphenothrin-IGR **Squeeze-On** for Dogs.

B. Challenge - Twenty-seven days after the first induction exposure 0.4 mL of a 75% w/w mixture of the test material in mineral oil was applied to a naive site on the right side of each guinea pig at a previously unexposed site. These sites were evaluated and scored for erythema at 24 and 48 hours after the challenge application.

C. Naive Controls - At the time the 20 previously induced guinea pigs were challenged, 10 previously unexposed (negative control) guinea pigs were similarly challenged.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Following challenge, 7/20 previously exposed guinea pigs showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours. 4/10 controls showed very slight (score of 0.5) erythema at 24 hours; all scored zero at 48 hours.

B. Positive control - The report includes results from a positive control study (PSL Study #12371) which was conducted with technical (85%) alpha-Hexylcinnamaldehyde and completed on August 15, 2002. The results (3/10 previously exposed, 0/5 naive control guinea pigs showing a positive response at challenge) were appropriate. The study dates for the testing with Cyphenothrin-IGR **Squeeze-On** for Dogs were from March 13 to April 11, 2003. While slightly outside the 6-month period indicated in the Guidelines, it is concluded the overall study findings are acceptable.

C. Reviewer's Conclusions: Cyphenothrin Squeeze-On for Dogs (containing 40% Cyphenothrin) is not a dermal sensitizer, based on the results from testing Cyphenothrin + IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen) is not a dermal sensitizer.

D. Deficiencies - The final date for the cited positive control study is approximately 7 months before the initiation of this study. However, TRB can accept the results of this study.

EPA Primary Reviewer: Byron T. Backus, Ph.D. Signature: _____
Technical Review Branch, Registration Division (7505C) Date_____
EPA Secondary Reviewer: William Dykstra, Ph.D. Signature: _____
Health Effects Division (7509C) Date_____

DATA EVALUATION RECORD

STUDY TYPE: Companion Animal Safety - Dogs OPPTS 870.7200

PC CODES: 129013 (Cyphenothrin), 129032 (Nylar), 105401 (Methoprene)
DP BARCODE: D305948 **RISK MANAGER:** (EPA): 13 **DECISION NO.:**338118

PRODUCT AND TEST MATERIAL: Cyphenothrin-IGR Spot-on for Dogs. [EPA File Symbol 2517-IN]; a liquid labeled "Gokilaht Spot-On w/IGR's (2824) 40.00% RS-Gokilaht; 3.00% S-Methoprene; 2.00% Nylar." According to a certificate of analysis (p. 47 of MRID 46166t08) the formulation contained 39.87% Gokilaht, 3.00% S-Methoprene and 2.00% Nylar. Packaged in unidose ampules containing t.5 mL product.

CITATION: Kuhn, J. (2003) Companion Animal Safety Study in Dogs: Cyphenothrin-IGR Spot-on for Dogs. Final Report. Project Number 7650/03. Unpublished study prepared by Stillmeadow, Inc. and Miller, Thomas A. 53 p. Study Completion Date: 20 October 2003. MRID 46166108.

SPONSOR: Sergeant's Pet Care Products, Inc. Omaha, NE 68130-1703.

EXECUTIVE SUMMARY: In a companion animal safety study (MRID 46166t08), groups of 12 dogs (from 5 to 9 males in each group) with each group including three t2-week old puppies weighing 4. t-6. t kg, 2 or 3 dogs weighing 6.8-15 kg, 3 or 4 dogs weighing t5.1-29.5 kg, and 3 weighing >29.5 kg) were dosed with: 1) the amount of vehicle contained in a single dose (Group I, controls); 2) at 1X the label use directions (except for puppies, which were dosed at t.5X) in Group II, and 3) at 5X the label use directions (except for puppies, which were dosed at 7.5X) in Group III. Group III dogs were treated five times with one hour between each treatment.

The test material was supplied in unidose 1.5 mL ampules. However, the report states that the mean volume delivered from one of these ampules was 1.17 mL. One dose for puppies consisted of material from a single 1.5 mL ampule (the proposed label states that dogs weighing less than t5 lbs [= 6.8 kg] are to be treated with t.0 mL), for dogs weighing 15-33 lbs (6.8-t5 kg) it was t.5 mL, for dogs weighing 15.1-29.5 kg it was the contents of two t.5 mL ampules (the proposed label says two 1.5 mL or one 3.0 mL ampule), and for dogs weighing >29.5 kg it was three 1.5 mL ampules (the proposed label says three 1.5 mL or one 4.5 mL ampules). The control material was supplied in bulk and placebo controls were treated with this formulation (without actives) at the rate of 55.13% of the active product dose volumes.

Administration was according to the proposed label directions and involved application of the test substance (or control vehicle) to the skin in a line along the spine starting at the back of the neck. Label directions specify application of the product as a spot-on or stripe treatment between the shoulder blades to dogs weighing up to t5 kgs. For dogs weighing between t5 and 29.5 kg application would be as a spot-on or stripe treatment at two sites on the back, one

between the shoulder blade and one directly in front of the base of the tail. For >29.5 kg the contents of one 1.5 mL ampule would be applied to the back as a spot-on or stripe between the shoulder, and the contents of the other two 1.5 mL ampules would be applied as a stripe on the back in front of the base of the tail.

Each dog in Groups I and II was observed at 1, 2, 3 and 4 hours following treatment on Day 0. Group III dogs were also observed "between the hourly dosings" (1, 2, 3, 4, 5, 6, 7 and 8 hours after the first treatment). All dogs were then observed twice (a.m. and p.m.) on Days 1-15.

Individual body weights were determined on Days -7, -3, 7 and 14. Individual food consumption was determined on a daily basis from Day -7 through Day 15 by measuring the amount of food given to each dog in the morning and subtracting the amount left at the end of the day. Blood samples were taken on Days -7 and 1 following overnight fasts.

Possible systemic effects related to exposure to the test material included ocular discharge and salivation. In the immediate period following treatment, ocular discharge was observed in one Group II dog (a puppy) at 4 hours post-dose, and in 4 Group III dogs (including all three puppies). Salivation (mostly very slight, but in some cases moderate) was observed in five Group III dogs (including 1/3 puppies), and was observed (very slight) in one adult 32.2 kg dog at 1 hour postdose (so at this time this dog had presumably been treated with only 1 or 2 applications of test material). Salivation was seen in another Group III adult starting at 3 hours, and in two additional Group III adults starting at 4 hours. During the subsequent 15-day observation period, ocular discharge was frequently observed (including continuously from day 10 to 15) in one control puppy, in none of the Group II (1X) dogs, and in one Group III puppy (days 1-2) and one Group III adult (days 1-6, then again on Days 13-15); both of these Group III animals had also shown ocular discharge in the period immediately following the first treatment. Salivation was observed in one Group III adult male at the AM observation on Day 1 (this dog had also showed salivation during the 8-hour period following the first treatment). One Group III male puppy showed a lesion (or lesions) on both sides of the shoulder (presumably at or near the application site) from Day 5 through 15, and was observed to scratch this area frequently.

Group III adults showed a mean weight loss between days -3 and +7. The incidences of adult dogs showing weight losses between days -3 and +7 were: Group I: 3/9; Group II: 4/9: Group III: 6/9. It is concluded then that for adult dogs exposure to a 5X dosage of test material was associated with a slight mean weight decrease in the period from Day -3 to Day 7.

While Group I puppies showed a greater mean weight gain in the period from Day -3 to +7 than Groups II and III, their mean weight gain/day in the subsequent period from Day 7 to 14 (0.053 kg/day) was comparable to the mean weight gains from Day -3 to +7 for Groups II (0.033 kg/day) and III (0.047 kg/day). Group III puppies also showed a greater mean weight gain in the period from Day -3 to 7 than did Group II puppies. There is no indication then that exposure to the test material affected body weight gain in puppies.

Puppies in Groups II and III showed lower mean food consumption values on Days 0 and 1 relative to their controls. This has to be considered as treatment-related. A similar effect in the adults was not evident.

No effects were noted on hematological or clinical chemistry parameters.

While the Guidelines for this type of study state that the targeted adequate margin of safety is 5X, it is also stated that: "Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)." The test material was not tested at 3X and effects were noted at 5X. However, the

effects noted at 5X, including ocular discharge (also noted in one puppy dosed at what was essentially 1.5X) and salivation were minimal (most occurrences of both ocular discharge and salivation were described as "very slight.") and reasonably transient. It is noteworthy that no systemic neurological signs (such as tremors or ataxia) were observed, and the salivation may have been due to ingestion of small amounts of test material from licking or biting the application area. In addition, the performing laboratory has demonstrated in the past extremely meticulous reporting of observational data in companion animal safety studies, and it is quite likely that these observations would not have been reported from some of the other laboratories which conduct this type of study.

For local dermal effects, one puppy treated at what was essentially a 7.5X dose level showed subsequent shoulder lesions and was noted to scratch this area frequently. Dermal exposure to pyrethroids can cause a burning and/or itching sensation at the application site, and this has to be considered an effect (unless the registrant can provide additional information demonstrating otherwise). However, this was an isolated case, and the three adult dogs treated with 3 unit doses/application with a total of 5 applications (for a total of fifteen 1.5-mL ampules in all) did not show a similar response.

However, one area of concern is that the 1.5 mL ampules (the only size tested in this study) delivered only an average of only 1.17 mL of test material, and the registrant is proposing packaging this product in 3.0 and 4.5 mL (as well as 1.0 and 1.5 mL) tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2 x 1.17) mL and the 4.5 mL tubes deliver no more than 3.51 (3 x 1.17) mL.

This study is classified as **Acceptable** as a companion animal safety study (OPPTS 870.7200) for puppies (12 weeks and older) and adult dogs. **It is concluded that there is an adequate margin of safety (at least 5X) between the exposure associated with the proposed use level for this formulation in dogs and that at which significant adverse systemic effects (not seen in this study, but which might include ear twitching, muscle tremors, drooling) may occur.** For dermal effects an effect was observed in one puppy in Group III (treated at essentially a 7.5X dose level), but in none of the other dogs (including the puppies in Group II), indicating a reasonably low potential for this effect in dogs treated at the proposed use level.

COMPLIANCE: Signed and dated Quality Assurance (p. 4), [No] Data Confidentiality (p. 2), and Good Laboratory Practice Compliance (p. 3) Statements were present.

I. MATERIALS

A. MATERIALS

1. Test material: Cyphenothrin-IGR Spot-on for Dogs, with a label declaration for active ingredients of RS-Gokilaht [=Cyphenothrin] (40.00%) , S-Methoprene (3.00%), and Nylar (2.00%). According to a certificate of analysis on p. 47 of MRID 46166108 the respective analytical values were 39.87%, 3.00% and 2.00%. Packaged in unit dose ampules containing 1.5 mL.
   Description: A liquid;
   Lot No.: #1683B
   Storage: Room Temperature

2. Administration: Topical (spot-on)

3. Vehicle control: X-5699-03 (Placebo Control); From Study 0310: Lot #03390A0100. liquid which was stored at room temperature.

4. Test animals
Species: Dog
Breed: From p. 9 of MRID 46166108: "Beagles and other breeds..."
Ages and weights at study initiation: "Animals were at least 3 months old at dosing. There were 3 animals from each group in each of the following weight ranges: <15, 15-33, 34-65 and >65 pounds (<6.8, 6.8-15, 15.1-29.5 and >29.5 kg). All dogs less than 15 pounds were pups that were 12 weeks old at dosing." [Note by reviewer: The alkaline phosphatase measurments from Dog 2854F (controls), 3085M (Group II) and 2156M (Group III) were relatively high - refer to pp. 32-34 - suggesting these were fairly young dogs too].
Sources: Butler Farms (Clyde, NY), Martin Creek Kennels (Wiliford, AR), Ridglan Farms (Mt. Horeb, WI) and STILLMEADOW, Inc.
Housing: Individually in kennels measuring 3' x 5.5'.
Diet: PMI Canine High Density Diet 5L18.
Water: Tap water, *ad libitum*
Environmental conditions:
Temperature: 22° ± 3°C
Humidity: 30 - 70%
Air changes: 10 - 12/hr
Photoperiod: 12 hr dark/12 hr light
Acclimation period: 2 weeks

II. STUDY DESIGN

A. IN LIFE DATES

From the report cover: study initiation date: 13 August 2003; study completion date: 20 October 2003.

B. ANIMAL ASSIGNMENT/ DOSAGE AND ADMINISTRATION

There were a total of 12 dogs per dosage group. Group 1 (1X vehicle; note: observation schedule on p. 16 of MRID 46166108 is the same for Groups 1 and 2, consistent with a single application of placebo on dogs in Group 1) consisted of 9 males and 3 females; Group II (1X) consisted of 5 males and 7 females, and Group III (5X) consisted of 8 males and 4 females. Assignment was on the basis of weight. From p. 10 of MRID 46166108: "Animals selected for testing were randomly assigned to three groups... Since there were three dose sizes (based on animal body weight) to be used in each treatment group, three dogs of each weight range were included in each group. The weight ranges were <15, 15-33, 34-65 and >65 pounds (<6.6, 6.8-15, 15.1-29.5 and >29.5 kg). The dogs <15 pounds were 3-month old puppies."

From p. 10 of MRID 46166108: "The test substance and placebo were applied to the skin in a line along the spine starting at the back of the neck. The test substance was supplied in unit dose plastic tubes, each containing 1.5 mL and were administered to each animal according to its body weight. The placebo control substance was provided in bulk. On Day 0, a label dose (1X) of the test substance was administered to each Group II animal according to body weight. Group III animals received the test substance at five times the label dose (5X) administered as single doses once every hour for 5 hours. The single dose volumes were: dogs <15 pounds, 1.5 mL (one unit dose); dogs 13 [15?]-33 pounds, 1.5 mL (one unit dose); dogs 34-65 pounds, 3 mL (two unit doses); and dogs >65 pounds, 4.5 mL (three unit doses). Group I was treated with the placebo control material in a volume equivalent to that of the normal label dose of the test substance less the volume of that dose that was occupied by the active ingredients]or approximately

55% of a normal 1X dose volume]..."

TABLE 1. Study design							
Group & Weight Range (kg)		Number of dogs or puppies		Cumulative Dose/dog			Number of applications
		Male	Female	Total/Dog	Mean mL/kg	Mean Dosage Cyphenothrin (mg/kg)[d]	
I (control)	<6.6[a]	3	0	0.83 mL[b]	0.16[b]	0	1
	6.8-15	1	1	0.83 mL[b]	0.08[b]	0	
	15.1-29.5	2	2	1.65 mL[b]	0.09[b]	0	
	>29.5	3	0	2.48 mL[b]	0.07[b]	0	
II (1X)	<6.6[a]	1	2	1.17 mL[c]	0.28[c]	112[d] [121][e]	1
	6.8-15	1	2	1.17 mL[c]	0.09[c]	36[d] [39][e]	
	15.1-29.5	1	2	2.34 mL[c]	0.12[c]	48[d] [52][e]	
	>29.5	2	1	3.51 mL[c]	0.11[c]	42[d] [45][e]	
III (5X)	<6.6[a]	1	2	5.85 mL[c]	1.26[c]	503[d] [543][e]	5
	6.8-15	0	2	5.85 mL[c]	0.51[c]	207[d] [224][e]	
	15.1-29.5	3	1	11.7 mL[c]	0.64[c]	255[d] [275][e]	
	>29.5	3	0	17.55 mL[c]	0.50[c]	199[d] [215][e]	

Data calculated from information on p. 14-15 in MRID 46166108.
[a] Puppies
[b] Placebo
[c] Test material (with actives); amount delivered based on 1.17 mL/application.
[d] Based on a specific gravity for the test material of 1.00 g/mL (consistent with the calculations for dosage as reported on pp. 14-15 of MRID 46166108) and based on 1.17 mL delivered/tube.
[e] Based on a specific gravity of 1.08 g/mL
Note: According to the CSF the specific gravity of the proposed product is about 1.08; assuming the product contains 40% Cyphenothrin then 1.5 mL would be 1.62 g and would contain 648 mg of Cyphenothrin. The calculations of dosage of Cyphenothrin in the report (see p. 14-15 of MRID 46166108) appear to be based on a specific gravity for the proposed product of about 1.00. Example: Dog 3067 F weighing 4.2 kg received one 1.5 mL dose of the product and this is reported as a dosage of 142 mg/kg Cyphenothrin. 142 mg/kg x 4.2 kg = 596.4 mg; dividing this by 0.3987 (the analytical percentage) gives 1496 mg (= 1.496 g) total product applied. However, in Appendix G (see p. 52 of MRID 46166108) it is stated that the unit dose containers did not deliver the entire target dose of 1.5 mL, as there was a mean delivered volume of 1.17 mL. A statement in Appendix G ("...5X dose rates ranged from 494 to 630 mg/kg for the smallest subjects.") is consistent with delivery of 1.17 mL/dose and a specific gravity of about 1.08 g/mL.

C. DOSE SELECTION RATIONALE

According to the proposed label this product will be packaged in unidose 1.0, 1.5, 3.0 and 4.5 mL applicator tubes. These correspond to single treatments for dogs weighing 15 lbs and under, 15-33 lbs, 33-66 lbs and >66 lbs. However, in this study, Group 2 (1X) dogs (puppies) weighing less than 15 lbs received 1.5 mL (instead of 1.0 mL), while Group 3 (5X) dogs (puppies) weighing less than 15 lbs received 5 x 1.5 mL = 7.5 mL (instead of 5 x 1.0 mL = 5.0 mL).

D. EXPERIMENTAL DESIGN

From p. 10 of MRID 46166108: "Each animal was observed at 1, 2, 3 and 4 hours following dosing on Day 0 and then twice daily [AM and PM] for the duration of the study. Group III animals were also observed between the hourly dosings. Each animal was examined for signs of any pharmacologic and/or toxicologic effects. Only abnormalities were recorded."

Individual dogs were weighed on Days -7, -3, 7 and 14.

Individual food consumption was measured daily by measuring the amount of food given to each dog in the morning and subtracting the amount of food left at the end of the day.

Baseline blood samples were collected from each dog on Day -7 by jugular venipuncture following an overnight fast. Blood samples were also similarly collected on Day 1.

E. PATHOLOGICAL PARAMETERS

Blood samples were collected on Study Days -7, and 1 by jugular venipuncture following an overnight fast. The CHECKED (X) parameters were examined:

a. Hematology

X		X	
X	Hematocrit (HCT)*	X	Leukocyte differential count*
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count		Reticulocyte count
	Blood clotting measurements		
	(Thromboplastin time)		
	(Clotting time)		
X	(Prothrombin time [PT])*		
X	(Activated partial thromboplastin time [APTT])*		
	Erythrocyte morphology		

*Recommended in OPPTS 870.7200 Guidelines.

b. Clinical chemistry

X	ELECTROLYTES	X	OTHER
X	Calcium*	X	Albumin (Alb)*
X	Chloride*	X	Blood creatinine (Crea)*
	Magnesium	X	Blood urea nitrogen (BUN)*
X	Phosphorus*		Total Cholesterol
X	Potassium*	X	Globulin (Glob)*
X	Sodium*	X	Glucose (Gluc)*
		X	Total and direct bilirubin (T Bil & D Bil)*
	ENZYMES	X	Total serum protein (TP)*
X	Alkaline phosphatase(ALPor ALK)*		Triglycerides
	Cholinesterase(ChE)		Serum protein electrophoresis
	Creatine kinase	X	Albumin/Globulin (A/G) ratio
	Lactic acid dehydrogenase(LDH)		
X	Serum alanine aminotransferase (ALT or SGPT)*		
X	Serum aspartate aminotransferase(AST or SGOT)*		
	Gamma glutamyl transferase(GGT)		
	Amylase		
	Glutamate dehydrogenase		

*Recommended in OPPTS 870.7200 Guidelines.

F. STATISTICS

The statistical report is found in Appendix G. It consists of a 6-page document (pages 48-53 of MRID 46166 t08). From p. 51 of MRID 46 t66108: "The data generated by the test facility...were statistically analyzed by Student's "t" test, assuming equal variances, using the statistical program in Microsoft Excel, version 97-SR-1... Since cyphenothrin is potentially the most toxic component of the product (pyriproxyfen and methoprene are known to be virtually mammalian-inert) cyphenothrin dosage was the focus. To ensure that some of the test subjects were treated at or above the target maximum dose rate of t00 mg of cyphenothrin per kg body weight, the t2-week-old Beagle pups were treated with the next higher unit dose volume. Although weighing between 9 and 11 lb at treatment, for which the proposed label dose rate is one dose of t mL, these pups received one 1.5 mL unit dose. To validate the dosage delivered to the principals, the expelled contents of six 1.5 mL unit dose containers were each weighed..." [Note: the report text then refers to Table 1.1, which is not present in the report]. From p. 52 of the report: "The dose validation data (Table 1.1) indicated that the unit dose containers, if filled at the target dose volume of t.5 mL, were not capable of delivering the entire target volume (mean volume delivered was t.17 mL).

G. DISPOSITION OF ANIMALS

Not stated. According to the OPPTS 870.7200 Guidelines: "Routine sacrifice or necropsy is not required for surviving animals."

H. COMPLIANCE

Signed and dated Quality Assurance [p. 4], [No] Data Confidentiality [p. 2], and Good Laboratory Practice (GLP) Compliance [p. 3] Statements were present.

III. RESULTS

A. EXPOSURE LEVELS

The dose per 1.17 mL application (based on a product specific gravity of 1.08 g/mL) is t.264 g. Since the test material contained (by analysis) 39.87% Cyphenothrin, 3.00% S-Methoprene and 2.00% Nylar, each 1.17 mL dose then contained 0.504 g (=504 mg) Cyphenothrin, 0.038 g (=38 mg) S-Methoprene and 0.025 g (=25 mg) Nylar. For Group II (tX) mean cumulative Cyphenothrin dosages were: puppies (<6.6 kg): 121 mg/kg; dogs 6.8-t5 kg: 39 mg/kg; dogs 15. t-29.5 kg: 52 mg/kg; and dogs >29.5 kg: 45 mg/kg. For Group III (5X) dosages were: puppies (<6.6 kg): 543 mg/kg; dogs 6.8-t5 kg: 224 mg/kg; dogs 15.1-29.5 kg: 255 mg/kg; and dogs >29.5 kg: 215 mg/kg. Refer to Table 1 of this DER. B. MORTALITY

There was no mortality, with all dogs surviving the 14-day observation period.

C. CLINICAL SIGNS

In the observation period immediately following treatment, no clinical signs of systemic toxicity were observed in Group I (controls). In Group II (1X) animal 3074 (a male pup weighing 4.1 kg) showed very slight ocular discharge from both eyes at 4 hours post-dose. In Group III (5X) four dogs (including all 3 puppies) showed very slight to moderate ocular discharge from one or both eyes in the period from one hour to 8 hours post-dosing. In addition, five dogs (including one puppy) showed very slight to moderate salivation during this period (in two dogs it was classified as very slight). Very slight salivation occurred in one animal at 1 hour (i.e., presumably following a single dosage of test material), and in two others it was first noted at 3 hours (after 3 application treatments)

Slight to moderate green ocular discharge (both eyes) was observed in one control puppy in the period from Day 1 to Day 6, and then again in this puppy from Day 10 to Day 15. No ocular discharge was observed in Group II in the period from Day 1 to Day 15. One Group III puppy showed clear ocular discharge from the left eye on Days 1 and 2, while an adult dog showed clear ocular discharge from the left eye from Day 1 through Day 6, then again from Day 13 through Day 15.

TABLE 2. Adverse Effects Observed in Dogs Treated with Cyphenothrin-IGR Spot-on In the Period Immediately Following Treatment[a]

Parameter	Group I (Control)	Group II (1X)	Group III (5X)
Ocular discharge - one or both eyes in the immediate post-dosing period	0[0[	1[1/48]	4[12/96]
Salivation	0[0]	0[0[	5[18/96]
Soft stool	0[0]	0	2[2/96]
Spiked greasy hair at application site in the immediate post-dosing period	0[0]	2[2/48]	0[0]

[a]Data taken from Table 2 (p. 15) of MRID 46166108.

From p. 11 of MRID 46166108: "Five of the Group II [1X] animals exhibited greasy spiked fur and/or white deposits at the dose site through Day 3. The only other observation noted in this group was moderate white foamy vomit in one dog on Day 8. In Group III, greasy and/or spiked fur and/or white deposits were seen through Day 1 in two dogs, through Day 3 in three dogs, through Day 6 in three dogs and [from Day 5] through Day 15 in one dog. Other observations included slight clear ocular discharge through Day 2 and shoulder lesions through Day 15 in one animal (the dog was observed to scratch the irritated area frequently), and slight to moderate diarrhea on Days 3 and 4 in another animal. Another dog had very slight to moderate clear ocular discharge through study termination with slight to moderate redness around the eye on Days 3-6. One dog exhibited slight salivation on Day 1 and moderate diarrhea on Day 14, and another had a lesion on the back on Days 7-15."

The Group III dog with the lesions on the shoulder (from p. 18: "both sides") from Day 5 through 15 was 3070M (a male puppy), treated with five 1.5 mL applications, while the Group III dog with the lesion on the back (Days 7-15) was 2853F (a female adult) also treated with five 1.5 mL applications.

D. BODY WEIGHT AND WEIGHT GAIN

From p. 12 of MRID 46166108: "The average weight gain[s] for Groups I, II and III were 1.1, 1.0 and 0.6 kilograms, respectively. There were no significant differences among groups, and no dose related responses."

The values in Table 3 are calculated from individual body weight data (p. 14-15 of MRID 46166108):

TABLE 3. Mean Body Weights for Dogs by Group

Group	kg ± S.D.				Mean Wt change Day -3 to 7	Mean Wt change Day -3 to 14
	Day -7	Day -3	Day 7	Day 14	kg ± S.D.	kg ± S.D.
I (Controls) puppies	4.63 ± 0.50	5.07 ± 0.93	6.13 ± 1.01	6.50 ± 1.10	1.07 ± 0.15	1.43 ± 0.31
I (Controls) adults	21.87 ± 9.93	22.34 ± 10.26	22.86 ± 10.90	23.31 ± 11.15	0.51 ± 0.87	0.97 ± 1.00
II (1X) puppies	4.80 ± 1.14	4.17 ± 0.06	4.50 ± 0.10	4.97 ± 0.31	0.33 ± 0.15	0.80 ± 0.36
II (1X) adults	21.64 ± 9.61	21.90 ± 9.16	22.53 ± 10.29	22.91 ± 10.29	0.41 ± 1.36	1.01 ± 1.61
III (5X) puppies	4.67 ± 0.71	4.63 ± 0.57	5.10 ± 0.70	5.63 ± 0.50	0.47 ± 0.15	1.00 ± 0.10
III (5X) adults	22.18 ± 10.00	22.38 ± 10.35	22.18 ± 10.40	22.86 ± 10.68	-0.20 ± 0.32	0.48 ± 0.58

Values calculated from data on p. 14 and 15 of MRID 46166108.

The possibility exists that there was a switch of puppies (or their bodyweights) as pup 3073M (assigned to controls) weighed 4.1 kg on day -7 but 6.1 kg on day -3, while pup 3074M (assigned to Group II or 1X) weighed 6.1 kg on day -7 but 4.1 kg on day -3. However, because this switch would have occurred before the dogs were treated, there would have been no impact on the study results.

The only group in which adults showed a mean weight loss between days -3 and +7 was Group III. The incidences of adult dogs showing weight losses between days -3 and +7 were the following: Group I: 3/9; Group II: 4/9: Group III: 6/9. It is concluded then that for adult dogs exposure to a 5X dosage of test material was associated with a slight mean weight decrease in the period from Day -3 to Day 7.

While Group I puppies showed a greater mean weight gain in the period from Day -3 to +7 than Groups II and III, their mean weight gain/day in the subsequent period from Day 7 to 14 (0.053 kg/day) was comparable to the mean weight gains from Day -3 to +7 for Groups II (0.033 kg/day) and III (0.047 kg/day). Group III puppies also showed a greater mean weight gain in the period from Day -3 to 7 than did Group II puppies. There is no indication then that exposure to the test material affected body weight gain in puppies.

TABLE 4. Mean Body Weight Gains for Puppies				
	Day -3 to +7	Day -3	Mean Pup Wt. Gain kg/Day Day -3 to +7	Mean Pup Wt. Gain kg/Day Day 7 to 14
I (Controls) puppies	1.07 ± 0.15	0.37 ± 0.15	0.107	0.053
II (1X) puppies	0.33 ± 0.15	0.47 ± 0.21	0.033	0.067
III (5X) puppies	0.47 ± 0.15	0.53 ± 0.25	0.047	0.076

Values calculated from data on p. 14 and 15 of MRID 46166108.

E. FOOD CONSUMPTION

Puppies in Groups II and III showed lower mean food consumption values on Days 0 and 1 relative to their controls. This has to be considered as treatment-related. A similar effect in the adults was not evident.

TABLE 5. Mean Diet ± S.D. (g) Consumed by Dog/Group by Day							
Group	Day -1	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5
I (Controls) puppies	227 ± 40	267 ± 14	263 ± 17	279 ± 27	315 ± 27	252 ± 41	275 ± 0
I (Conirols) adults	431 ± 129	475 ± 131	525 ± 110	496 ± 138	504 ± 166	313 ± 173	496 ± 146
II (1X) puppies	193 ± 7	122 ± 3	89 ± 17	239 ± 45	200 ± 81	165 ± 11	209 ± 15
II (1X) adults	384 ± 218	387 ± 202	339 ± 248	410 ± 207	435 ± 216	310 ± 177	418 ± 192
III (5X) puppies	234 ± 27	85 ± 0	98 ± 82	201 ± 69	178 ± 51	167 ± 98	191 ± 0
III (5X) adults	445 ± 141	497 ± 122	379 ± 207	452 ± 175	435 ± 159	322 ± 236	437 ± 122

Values calculated from data on p. 26-29 of MRID 46166108.

F. HEMATOLOGY

From p. 12 of MRID 46166108: "The hematology values were within normal limnits except for platelet counts, prothrombin time and/or activated partial thromboplastin time. These values were significantly elevated in all groups, including the placebo group, and therefore were not dose related."

There were no indications of any treatment related effects on hematology parameters. Alkaline phosphatase activity was elevated for puppies in all groups (and was usually above the reference range of 10-150 IU/L), but this is normal for puppies.

G. CLINICAL CHEMISTRY

There were no indications of any treatment related effects on clinical chemistry parameters. As indicated on p. 12 of MRID 46166108 clinical chemistry results "were within normal limits in males and females and the few significant differences among male or female means in any group or between group means did not appear to be related to treatment with the test substance."

H. NECROPSY FINDINGS

As there were no mortalities, there were no necropsy findings.

IV. DISCUSSION

Possible effects related to exposure to the test material included ocular discharge (seen in both eyes of one puppy in Group II at 4-hours post-dosing; classified as very slight; seen in 3 puppies and one adult in Group III in the period from one hour to eight hours following the first dose. In all 3 puppies ocular discharge, when it occurred during this period, was described as very slight. In the adult there was progression to a red, irritated, watery left eye at 8 hours following the first dosage. In addition, very slight to moderate salivation was noted in five dogs (including two puppies) of Group III in the one to eight hours following treatment. Salivation was seen in one adult (#3080, a 32.2-kg male receiving three 1.5-mL doses at each application) at the one hour observation (i.e., presumably one hour after the first treatment), and very slight salivation was seen in this one dog at 3 and 4 hours [following the first dosage], and then moderate salivation was seen at 8 hours. However, no effects ["No Observable Abnormalities"] were then seen in this dog for the remainder of the 14-day observation period.

Adult dogs dosed at the 5X level tended to show a slight mean weight loss in the week following treatment, although there was no indication of an effect on food consumption.

There was no indication of an effect on body weight in puppies at the 1X and 5X dose levels [actually 1.5X and 7.5X dose levels], although their mean food consumption levels for days 0 and 1 were noticeably lower than concurrent values of their controls as well as their own pre-exposure food consumption.

While the Guidelines for this type of study state that the targeted adequate margin of safety is 5X, it is also stated that: "Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)." The test material was not tested at 3X and effects were noted at 5X. However, the effects noted at 5X, including ocular discharge (also noted in one puppy dosed at what was essentially 1.5X) and salivation were minimal (most occurrences of both ocular discharge and salivation were described as "very slight.") and reasonably transient. It is noteworthy that no systemic neurological signs (such as tremors or ataxia) were observed, and the salivation may have been due to ingestion of small amounts of test material from licking or biting the application area. In addition, the performing laboratory has demonstrated in the past extremely meticulous reporting of observational data in companion animal safety studies, and it is quite likely that these observations would not have been reported from some of the other laboratories which conduct this type of study.

For local dermal effects, one Group III puppy (treated at what was essentially a 7.5X dose level) showed subsequent shoulder lesions (from day 5 through 15) and was noted to scratch this area frequently. Dermal exposure to pyrethroids can cause a burning and/or itching sensation at the application site, and this has to be considered an effect (unless the registrant can provide additional information demonstrating otherwise). However, this was an isolated case, and the three adult dogs treated with 3 unit doses/application with a total of 5 applications (for a total of fifteen 1.5-mL ampules in all) did not show a similar response.

However, one area of concern is that the 1.5 mL ampules (the only size tested in this study) delivered only an average of only 1.17 mL of test material, and the registrant is

proposing packaging this product in 3.0 and 4.5 mL (as well as 1.0 and 1.5 mL) tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2 x 1.17) mL and the 4.5 mL tubes deliver no more than 3.51 (3 x 1.17) mL.

This study is classified as **Acceptable** as a companion animal safety study (OPPTS 870.7200) for puppies (12 weeks and older) and adult dogs. **It is concluded then that there is an adequate margin of safety (at least 5X) between the exposure associated with the proposed use level for this formulation in dogs and the dose at which significant adverse systemic toxicological effects (not seen in this study, but which might include ear twitching, muscle tremors, drooling) may occur.** For dermal effects an effect was observed in one puppy in Group III (treated at essentially a 7.5X dose level), but in none of the other dogs in this study (including the puppies in Group II), indicating a reasonably low potential for this effect in dogs treated at the proposed use level.

STUDY DEFICIENCIES: The test material was not tested at 3X and effects were noted at 5X. However, the effects noted at 5X, including ocular discharge (also noted in one puppy dosed at what was essentially 1.5X) and salivation were minimal (most occurrences of both ocular discharge and salivation were described as "very slight."). In addition, the performing laboratory has demonstrated in the past extremely good reporting of observational data, and it is quite possible that what was reported in this study would not have been reported from some of the other laboratories which conduct this type of study.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D305953
2. **PC CODES:** 129013 Cyphenothrin, 129032 Pyriproxyfen, 105401 Methoprene
3. **CURRENT DATE:** November 23, 2004
4. **TEST MATERIAL:** Cyphenothrin-IGR Squeeze-On for Dogs, a clear light yellow liquid with a specific gravity of 1.061 g/mL containing 39.87% Cyphenothrin, 3.00% Methoprene and 2.00% Nylar (Pyriproxyfen). For this action, the test material is being used to support the registration of a product containing 40% Cyphenothrin as sole active ingredient.

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/Product Safety Labs (New Jersey)/Project No. 13320/20-MAY-2003	46166103	LD_{50}>2000 mg/kg. Up and down method defaulting to acute tox class method. 2/5 Sprague-Dawley derived female rats died within 24 hrs after dosage at 2000 mg/kg; two rats which survived showed reduced fecal volume, ventral staining and hypoactivity, with recovery by day 4. All survivors gained weight in the period from day 0 to 7 and again from day 7 to 14. Postmortem necropsy of rats which died showed discoloration of the lungs and intestines and fluid-filled stomachs. Findings from rats which survived to terminal sacrifice were unremarkable.	III	A
Acute dermal toxicity/rat/ Product Safety Labs (New Jersey)/Project No. 13321/20-MAY-2003	46166104	LD_{50} > 2000 mg/kg. 5M & 5F Sprague-Dawley derived albino rats were dermally exposed to 2000 mg/kg for 24 hrs; no mortality, no signs of systemic toxicity. Three males had some dermal irritation with clearing by Day 2. All rats gained wt from day 0 to 7 and from day 7 to 14. No gross abnormalities were observed at post-sacrifice necropsy.	III	A
Primary eye irritation/rabbit/ Product Safety Labs (New Jersey)/Project No. 13322/20-MAY-2003	46166105	No corneal opacity. 3/3 rabbit eyes were positive (grade 2) for conjunctival irritation at 1 and 24 hrs. All eyes clear (all scores zero) by 72 hrs.	III	A
Primary dermal irritation/rabbit/ Product Safety Labs (New Jersey)/Project No. 13323/20-MAY-2003	46166106	No edema (all scores for edema = 0). All 3 sites scored 1 for erythema at 1 hr and 2 at 24, 48 and 72 hrs. One site scored 2 for erythema on day 7 while the other two scored 1. All scores zero on dat 10. The PII (average of scores at 1, 24, 48 & 72 hrs) = 1.75	IV	A
Dermal sensitization (Buehler method)/guinea pig/Product Safety Labs (New Jersey	46166107	No indication that test material is a dermal sensitizer.	Not a sensitizer	A

Companion animal/adult dog & 12-wk old puppies/ Stillmeadow TX/Project No. 7650/03/20-OCT-2003	46166108	Three groups of dogs, each containing 9 adults & three 12-week old puppies: Group I (control) was treated with the amount of vehicle at 1X; Group II was treated at 1X (dogs 6.8-15 kg: contents from one 1.5 mL ampule; 15.1-29.5 kg: contents of two 1.5 mL ampules; >29.5 kg: contents of three 1.5 mL ampules. Puppies (<6.8 kg) were treated with contents of one 1.5 mL ampule (1.5X). Group III adults were treated at 5X (with treatments at 1-hr intervals) and Group III pups were treated at 7.5X label dose. Administration was as a spot-on and/or stripe treatment on the back. Possible systemic effects noted following administration were ocular discharge in one Group II puppy at 4 hrs post-dose and in 4 Group III animals (including all 3 puppies). Salivation was also noted in 5 Group III dogs in the period (1-8 hrs) following first administration of test material. Puppies (but not adults) showed of Groups II and III also showed lower mean food consumption on days 0 and 1. One Group III puppy showed shoulder lesions (presumably in the area where test material was applied) from day 5 to the end of the study and was noted to scratch this area frequently. No effects on clinical chemistry or hematology parameters. One concern is that 1.5 mL ampules delivered only 1.17 mL test material; registrant is proposing packaging this product in 3.0 & 4.5 mL tubes. This is acceptable only if the 3.0 mL tubes deliver no more than 2.34 (2x1.17)mL and the 4.5 mL tubes deliver no more than 3.51 (3x1.17)mL.	N/A	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated

FEE

DATE OUT: 03/FEB/2005

FEE: PRODUCT CHEMISTRY REVIEW OF: Manufacturing-Use [ ] End-Use Product [X]
DP BARCODE: D305951 **EPA RECEIVED DATE:** 27/JUL/2004 **FILE SYMBOL/REG:** 2517-IL
PRODUCT: Sergeant's Cyphenothrin Squeeze-On For Dogs **MRIDs** #463038-01 & -02 **ACTION** R31
COMPANY : Sergeant's Pet Care Products, Inc. **NON-FOOD USES** [X] **DECISION NO.:** 345654
PPC NUMBER OF THE TGAI IN THE PRODUCT: 129013

FROM: Sami Malak, Chemist
Technical Review Branch/RD (7505C)

TO: 13 George LaRocca/Linda DeLuise
Insecticide Branch/RD (7505C)

INTRODUCTION:

In a letter dated 16/JUN/2004, Brazos Associates, Inc. an agent for the applicant requested registration of subject product. In support of this action, the applicant included product chemistry data, a proposed label EPA received on 20/JUN/2004, a proposed basic CSF dated 16/JUN/2004, Formulator's Exemption, Certificate with respect to Citation of Data, and data Matrix..

FINDINGS:

1a. The subject product was produced by a non-integrated formulation system, meaning that the active ingredient in the product is registered. The product contains 40% Cyphenothrin, Reg. No. [redacted]

1b. The subject product, an insecticide, is intended for insect control infesting dogs and puppies older than 12 weeks.

2a. The applicant should be advised to submit product chemistry data requirements pertaining to the storage stability (GRN 830.6317) and corrosion characteristics (GRN 830.6320) identified in this memorandum as data gaps.

2b. Except for the data gaps in Finding 2(a) above, the submitted/referenced product chemistry data is adequate and support registration of subject product.

3. Adequate analytical method is available for enforcement. The method was previously submitted and reviewed in connection with registration of the technical sources, Cyphenothrin, Reg. No. [redacted].

4. The label claim nominal concentrations of 40% Cyphenothrin is consistent with that in the submitted basic CSF dated 16/JUN/2004, both are in compliance with the regulations of PR Notice 91-2. Further, the storage and disposal statement and the physical or chemical hazards statement are in compliance with the regulations of 40CFR§156.78.

5. The proposed basic CSF dated 16/JUN/2004, was filled out correctly in compliance with the regulations of PR Notice 91-2. Further, the upper and lower certified limits are within the standard limits of 40CFR§158.175(b)(2). All ingredients claimed in the CSF are cleared for use in pesticide formulations intended for non-food uses.

CONCLUSIONS: After resolving Findings 2(a) above, the TRB will have no objections for registration of subject product.

REVIEW OF PRODUCT CHEMISTRY DATA:

1. A statement of data confidentiality dated 16/JUN/2004 was included with this submission claiming confidentiality of some of the submitted data on the basis of its falling within the scope of FIFRA§10(d)(1)(A), (B), or (C). Review of CBI data has been removed to Confidential Appendix A.

2. A GLP statement dated 23/JUN/2004 was included with this submission to the effect that some of the submitted studies were conducted in compliance with the GLP requirements of 40CFR§160.

DATA SUBMITTED

Group A, Series 830-Product Identity, Composition, and Analysis (40 CFR 155, 160, 162, 167, 175 & 180)

830-1550 Product Identity and Composition

This product contains one registered technical grade of an active ingredient plus cleared inert ingredients intended for non-food uses (refer to product's basic CSF dated 16/JUN/2004).

830-1600 Description of Materials Used to Produce the Product:
Refer to Confidential appendix A.

830-1650 Description of Formulation Process:
Refer to Confidential appendix A.

830-1670 Discussion of Formation of Impurities:
Refer to Confidential appendix A.

830-1700 Preliminary Analysis:
Refer to Confidential appendix A.

830-1750 Certified Limits:
Refer to Confidential appendix A.

830-1800 Enforcement Analytical Method:

Adequate analytical method is available for enforcement. The method was previously submitted and reviewed in connection with registration of the technical sources, Cyphenothrin, Reg. No. [redacted].

Identity, Composition, Formulation, and Analysis, Subgroup A, Series 830.1550 to 830.1800 (40 CFR 158.155 to 158.180)

Guideline Reference NO.(GRN 830.)/Title	Data Fulfilled	MRID No.
.1550 Product identity and composition	Y	463038-01
.1600 Description of materials used to produce the product	Y	463038-01
.1650 Description of formulation process	Y	463038-01
.1670 Discussion of formation of impurities	Y	463038-01
.1700 Preliminary analysis	Y	463038-01
.1750 Certified limits	Y	463038-01
.1800 Enforcement analytical method	Y	463038-01

Physical and Chemical Properties, Subgroup B, Series 830.6302 to -830.7300 (40 CFR 158.190)

Guideline Reference NO.(GRN 830.)/Title	Data Fulfilled	Value or Qualitative Description	MRID No.
.6302 Color	Y	Clear golden yellow.	463038-02
.6303 Physical state	Y	Liquid.	463038-02
.6304 Odor	Y	Sharp sweet smell, slightly irritating.	463038-02
.6314 Oxidation/seduction: Chemical incompatibility	NA	Does not contain an oxidising or reducing agents.	
.6315 Flammability/flame extension	Y	>200°F.	463038-02
.6316 Explodability	NA	Not considered to be explosive.	
.6317 Storage stability	G		
.6319 Miscibility	Y	Completely miscible in aromatics, petroleum distillates and alcohols. Immiscible in water.	463038-02
.6320 Corrosion characteristics	G		
.6321 Dielectric breakdown voltage	NA	It is not recommended for use around electrical equipment.	
.7000 pH	NA	Insoluble in water.	
.7100 Viscosity	Y	94.5 cps @ 23°C.	463038-02
.7300 Density/relative density/bulk density	Y	1.076 @ 20°C.	463038-02

Explanations: Y =The requirements were fulfilled; N = The requirements not fulfilled; N/A = Not applicable; G = Data gap; U = Requires upgrading; I = Incomplete or in progress; W = Waived.

Confidential Appendix A

830-1600 Description of Materials Used to Produce the Product:

One registered technical grade of an active ingredient plus cleared inert ingredients intended for non-food uses (refer to product's basic CSF dated 12/OCT/2004).

830-1650 Description of Formulation Process:

[redacted]

830-1670 Discussion of Formation of Impurities:

The applicant reported no impurities $\geq$0.1% by weight were known to be formed during formulation and storage of the product. There was no chemical reaction in the process.

830-1700 Preliminary Analysis:

The submitted results of preliminary analysis agree with the label claim nominal concentrations of the active ingredients in the product.

830-1750 Certified Limits:

The applicant reported the same certified limits as those in product's CSF, a basic formulation dated 16/JUN/2004.

cc:S. Malak and Central File (Reg. No. 2517-IL).
7505C:RD:TRB:CM-2:Rm.268:s.m.03/FEB/2005:703-308-9365: <2517-IL.>.

[MASTER CARTON/PACK LABEL - FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On For Dogs

• **DO NOT USE ON CATS [Box/Icon with Cat Image and Cross-Out]**
[• Pleasant Fresh Scent [or][Fragrance]]
[• Flea & Tick Control for Dogs & Puppies 12 weeks old and older]
[• ?? {?? - dependent on applicator size and quantity in market package - "e.g.3, 6 or 12 Months"}Supply][For Dogs Weighing Up To ?? Lbs.]
[• Three Way Protection [Kills fleas, ticks, and mosquitoes]] [for up to 42 days] [per application]
[•Three Way Protection to [Kills fleas, ticks, and mosquitoes]]
[•3 Way Protection! Kills ticks, & mosquitoes]
[• Extended Protection] [[42-Day] [6 Week] [Flea ,Tick & Mosquito Treatment]
[• 42-Day Flea and Tick Control]
[• For Dogs & Puppies (Over 12 Weeks of Age) Less than 15 lbs.]
[• For Dogs & Puppies (Over 12 Weeks of Age) 15 to 33 lbs.]
[• For Dogs & Puppies (Over 12 Weeks of Age) 33 to 66 lbs.]
[• For Dogs & Puppies (Over 12 Weeks of Age) 66 lbs and Over]
[• Three Applications {for cartons with 3 applicators}.] and/or [4-1/2 Month Supply] or [18 Week Supply]
[• For Dogs [less than 15 lbs.] or [15 lbs. to 33 lbs.] or [33 lbs. to 66 lbs.] or [66 lbs. and Over]
[• Best if used year round!]
[• Kills & Repels Fleas Up to [6 weeks], [42 days!]
[• Kills & Repels New Fleas in less than 1 hour!]
[• Kills & Repels New Ticks in less than 3 hours!]
[• Kills & Repels 95% of Fleas and Ticks [and continues to work for up to six weeks]
[• Kills 99% of Fleas one day after application]
[• Prevents ticks from attaching and feeding within 3 hours after application]
[• 95% efficacy against ticks for up to[6 weeks] [42 days]
[• Kills and Detaches Ticks]
[• Kills over 95% of Ticks]
[• Easy to Use Application]
[• Specially Formulated for Dogs and Puppies]
[• Patented Technology [combines effectiveness with gentleness!]]
[• 42 Day Protection!]
[• Monthly Calendar Stickers Inside!]
[• Kills Mosquitoes for up to [30 days!] [42 days!]
[• Kills Mosquitoes (vector of West Nile Virus) for up to [30 days] [42 days!]

[• Protects Against Blood Feeding by Mosquitoes (vector of Heartworm) For up to [30 days!] [42 days!]
[• Kills & Repels Ticks for Up to [42 days],[6 weeks]!]
[• Kills & Repels Deer Ticks (vector of Lyme Disease) for up to [35 days!] [42 days!]
[• Kills & Repels Ticks (Including Deer Ticks) for up to [35 days!] [42 days!]
[• Kills & Repels Brown Dog Ticks [(*Rhipicephalus sanguineus*)] for up to 42 days!]
[• Kills & Repels American Dog Ticks [(*Dermacentor variabilis*)] for up to 42 days!]
[• Apply every [42 days], [6 weeks]!]
[• 42 Days Flea and Tick Treatment!]
[• Kills & Repels Fleas and Ticks for up to 42 days!]
[• Kills & Repels Mosquitoes that are vectors of West Nile Virus.]
[• Waterproof formula.]
[• Dogs can be bathed 24 hours after squeeze-on is applied]
[• Continues to work 50% longer than other leading brands]
[• Longest lasting, quick acting]

[• May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[ ] - Denotes Optional Statements and/or Images that May be Used on Front, Back or Side Label Panels.

ACTIVE INGREDIENTS:
Cyphenothrin (CAS# 39515-40-7) 40.0%
OTHER INGREDIENTS: 60.0%
TOTAL: 100.0%

KEEP OUT OF REACH OF CHILDREN
CAUTION
See [Back][or][Side] Label Panel[s] for Additional Precautionary Statements

NET CONTENTS: **[THREE][SIX][TWELVE] 1.0 ml Tubes**
[THREE][SIX][TWELVE] 1.5 ml Tubes
[THREE][SIX][TWELVE] 3.0 ml Tubes
[THREE][SIX][TWELVE] 4.5 ml Tubes

[MASTER CARTON/PACK LABEL - BACK/SIDE PANELS]

Sergeant's Cyphenothrin Squeeze-On For Dogs

[DO NOT USE ON CATS] [Box/Icon with Cat Image and Cross-Out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling. FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with a mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Immediately call a poison control center or doctor. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give **any** liquid to the person. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.

HOTLINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS [or][x-xxx-xxx-xxxx] for emergency medical treatment information.

NOTE TO PHYSICIAN OR VETERINARIAN

Treat patient symptomatically

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, snap or cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 15 lbs. and Under: {For cartons containing 1.0 ml applicator tubes}
Apply one tube (1.0 ml) as a spot or stripe to the dog's back between the shoulder blades.

For Dogs Weighing Between 15 and 33 lbs. {For cartons containing 1.5 ml applicator tubes}
Apply one tube (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades.

For Dogs Weighing Between 33 and 66 lbs. {For cartons containing at least two 1.5 ml applicator tubes, or at least one 3.0 ml applicator tube}
[Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the second tube as a spot or stripe to the dog's back directly in front of the base of the tail.] - or - [Apply one tube (3.0 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.]

For Dogs Weighing 66 lbs. and Over: {For cartons containing at least three 1.5 ml applicator tubes, or at least one 4.5 ml applicator tube}
[Apply the first tube (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml each) along the dog's back extending to directly in front of the base of the tail.] - or - [Apply one tube (4.5 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in from of the base of the dog's tail.]

[MASTER CARTON/PACK LABEL - BACK/SIDE PANELS]

STORAGE AND DISPOSAL

STORAGE: Do not remove tube from the pack until ready to use. Store in a cool (below 25°C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

DISPOSAL: If empty: Do not reuse this container. Place in trash or offer for recycling if available. **If partly filled:** Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On For Dogs is an effective and easy to use product.] [Sergeant's Cyphenothrin Squeeze-On For Dogs has demonstrated that greater than 95% control of fleas and ticks are killed within one day of application.] [As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On For Dogs should be used as part of a program aimed at reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

[www.sergeants.com]

MADE IN
USA

[Sergeant's is committed to providing high quality products. If you have questions or comments about this product, please write: Sergeant's Consumer Response; P.O. Box 540399; Omaha, NE 68154-0399.]

[Satisfaction Guaranteed!] [Please return for a refund if not completely satisfied!]

[In Case of Emergency, call 1-800-224-PETS.]

[WARRANTY: SERGEANT'S PET CARE PRODUCTS, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENTS MADE ON THIS LABEL.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130
EPA Reg. No. 2517 -XX
EPA Est. No. XXXXX -XX -XXX

[BAR CODE AREA]

[TUBE/APPLICATOR LABEL]

FRONT PANEL -

Sergeant's Cyphenothrin Squeeze-On For Dogs, [Box/Icon with Cat Image and Cross-Out], [1.0 ml] or [1.5 ml] or [3.0 ml] or [4.5 ml], Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%

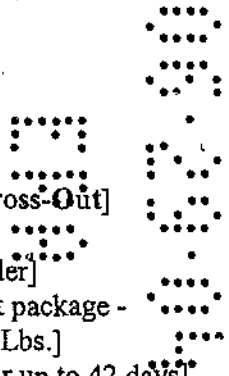
BACK PANEL -

READ DIRECTIONS/PRECAUTIONS BEFORE USING. CAUTION: KEEP OUT OF REACH OF CHILDREN EPA REG. NO. 2517-XX

Revised 06/16/2004:
S:\Main\Sergeant's Pet Products\Labels\Sergeant's Cyphenothrin Squeeze-On For Dogs.

[MASTER CARTON/PACK LABEL - FRONT PANEL]

Sergeant's Cyphenothrin Squeeze-On For Dogs



• **DO NOT USE ON CATS [Box/Icon with Cat Image and Cross-Out]**
[• Pleasant Fresh Scent [or][Fragrance]]
[• Flea & Tick Control for Dogs & Puppies 12 weeks old and older]
[• ?? {?? - dependent on applicator size and quantity in market package - "e.g.3, 6 or 12 Months"}Supply][For Dogs Weighing Up To ?? Lbs.]
[• Three Way Protection [Kills fleas, ticks, and mosquitoes]] [for up to 42 days] [per application]
[•Three Way Protection to [Kills fleas, ticks, and mosquitoes]]
[•3 Way Protection! Kills ticks, & mosquitoes]
[• Extended Protection] [[42-Day] [6 Week] [Flea ,Tick & Mosquito Treatment]
[• 42-Day Flea and Tick Control]
[• For Dogs & Puppies (Over 12 Weeks of Age) Less than 15 lbs.]
[• For Dogs & Puppies (Over 12 Weeks of Age) 15 to 33 lbs.]
[• For Dogs & Puppies (Over 12 Weeks of Age) 33 to 66 lbs.]
[• For Dogs & Puppies (Over 12 Weeks of Age) 66 lbs and Over]
[• Three Applications {for cartons with 3 applicators}.] and/or [4-1/2 Month Supply] or [18 Week Supply]
[• For Dogs [less than 15 lbs.] or [15 lbs. to 33 lbs.] or [33 lbs. to 66 lbs.] or [66 lbs. and Over]
[• Best if used year round!]
[• Kills & Repels Fleas Up to [6 weeks], [42 days!]
[• Kills & Repels New Fleas in less than 1 hour!]
[• Kills & Repels New Ticks in less than 3 hours!]
[• Kills & Repels 95% of Fleas and Ticks [and continues to work for up to six weeks]
[• Kills 99% of Fleas one day after application]
[• Prevents ticks from attaching and feeding within 3 hours after application]
[• 95% efficacy against ticks for up to[6 weeks] [42 days]
[• Kills and Detaches Ticks]
[• Kills over 95% of Ticks]
[• Easy to Use Application]
[• Specially Formulated for Dogs and Puppies]
[• Patented Technology [combines effectiveness with gentleness!]]
[• 42 Day Protection!]
[• Monthly Calendar Stickers Inside!]
[• Kills Mosquitoes for up to [30 days!] [42 days!]
[• Kills Mosquitoes (vector of West Nile Virus) for up to [30 days] [42 days!]

[• Protects Against Blood Feeding by Mosquitoes (vector of Heartworm) For up to [30 days!] [42 days!]
[• Kills & Repels Ticks for Up to [42 days],[6 weeks]!]
[• Kills & Repels Deer Ticks (vector of Lyme Disease) for up to [35 days!] [42 days!]
[• Kills & Repels Ticks (Including Deer Ticks) for up to [35 days!] [42 days!]
[• Kills & Repels Brown Dog Ticks [(*Rhipicephalus sanguineus*)] for up to 42 days!]
[• Kills & Repels American Dog Ticks [(*Dermacentor variabilis*)] for up to 42 days!]
[• Apply every [42 days], [6 weeks]!]
[• 42 Days Flea and Tick Treatment!]
[• Kills & Repels Fleas and Ticks for up to 42 days!]
[• Kills & Repels Mosquitoes that are vectors of West Nile Virus.]
[• Waterproof formula.]
[• Dogs can be bathed 24 hours after squeeze-on is applied]
[• Continues to work 50% longer than other leading brands]
[• Longest lasting, quick acting]

[• May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

[ ] - Denotes Optional Statements and/or Images that May be Used on Front, Back or Side Label Panels.

ACTIVE INGREDIENTS:	
Cyphenothrin (CAS# 39515-40-7)	40.0%
OTHER INGREDIENTS:	60.0%
TOTAL:	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See [Back][or][Side] Label Panel[s] for Additional Precautionary Statements

NET CONTENTS: **[THREE][SIX][TWELVE] 1.0 ml Tubes**
[THREE][SIX][TWELVE[1.5 ml Tubes
[THREE][SIX][TWELVE] 3.0 ml Tubes
[THREE][SIX][TWELVE] 4.5 ml Tubes

[MASTER CARTON/PACK LABEL - BACK/SIDE PANELS]

Sergeant's Cyphenothrin Squeeze-On For Dogs

[DO NOT USE ON CATS] [Box/Icon with Cat Image and Cross-Out]

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 12 WEEKS OF AGE.
DO NOT USE ON CATS

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling. FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 12 weeks of age. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. DO NOT USE ON CATS or animals other than dogs. Cats that actively groom or engage in close physical contact with treated dogs may be at risk of serious harmful effects. Sensitivities may occur after using ANY pesticide product on pets. If signs of sensitivity occur bathe your dog with a mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Immediately call a poison control center or doctor. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give **any** liquid to the person. • Do not give anything by mouth to an unconscious person.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.

HOTLINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-224-PETS [or][x-xxx-xxx-xxxx] for emergency medical treatment information.

NOTE TO PHYSICIAN OR VETERINARIAN

Treat patient symptomatically

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT USE ON CATS. May be toxic and potentially fatal if applied to or ingested by cats.

How to apply: Remove product tube from package. Holding tube with top end pointing up and away from face and body, snap or cut off top end. Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. Repeat application may be made if necessary, but do not apply more often than once every 4 weeks.

For Dogs Weighing 15 lbs. and Under: {For cartons containing 1.0 ml applicator tubes}
Apply one tube (1.0 ml) as a spot or stripe to the dog's back between the shoulder blades.

For Dogs Weighing Between 15 and 33 lbs. {For cartons containing 1.5 ml applicator tubes}
Apply one tube (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades.

For Dogs Weighing Between 33 and 66 lbs. {For cartons containing at least two 1.5 ml applicator tubes, or at least one 3.0 ml applicator tube}
[Apply two tubes (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the second tube as a spot or stripe to the dog's back directly in front of the base of the tail.] - or - [Apply one tube (3.0 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the dog's tail.]

For Dogs Weighing 66 lbs. and Over: {For cartons containing at least three 1.5 ml applicator tubes, or at least one 4.5 ml applicator tube}
[Apply the first tube (1.5 ml) as a spot or stripe to the dog's back between the shoulder blades and apply the contents of the other two tubes (1.5 ml each) along the dog's back extending to directly in front of the base of the tail.] - or - [Apply one tube (4.5 ml) as a continuous stripe on the dog's back starting between the shoulder blades and ending directly in from of the base of the dog's tail.]

[MASTER CARTON/PACK LABEL - BACK/SIDE PANELS]

STORAGE AND DISPOSAL

STORAGE: Do not remove tube from the pack until ready to use. Store in a cool (below 25°C) dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

DISPOSAL: If empty: Do not reuse this container. Place in trash or offer for recycling if available. **If partly filled:** Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

[Sergeant's Cyphenothrin Squeeze-On For Dogs is an effective and easy to use product.] [Sergeant's Cyphenothrin Squeeze-On For Dogs has demonstrated that greater than 95% control of fleas and ticks are killed within one day of application.] [As with all flea and tick control products, Sergeant's Cyphenothrin Squeeze-On For Dogs should be used as part of a program aimed at reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]

[www.sergeants.com]

MADE IN
USA

[Sergeant's is committed to providing high quality products. If you have questions or comments about this product, please write: Sergeant's Consumer Response; P.O. Box 540399; Omaha, NE 68154-0399.]

[Satisfaction Guaranteed!] [Please return for a refund if not completely satisfied!]

[In Case of Emergency, call 1-800-224-PETS.]

[WARRANTY: SERGEANT'S PET CARE PRODUCTS, INC. MAKES NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR OTHERWISE, EXPRESSED OR IMPLIED, CONCERNING THIS PRODUCT OR ITS USES WHICH EXTEND BEYOND THE USE OF THE PRODUCT UNDER NORMAL CONDITIONS IN ACCORDANCE WITH THE STATEMENTS MADE ON THIS LABEL.]

Made in the USA For:
Sergeant's Pet Care Products, Inc.
Omaha, NE 68130
EPA Reg. No. 2517 -XX
EPA Est. No. XXXXX -XX -XXX

[BAR CODE AREA]

[TUBE/APPLICATOR LABEL]

FRONT PANEL -

Sergeant's Cyphenothrin Squeeze-On For Dogs, [Box/Icon with Cat Image and Cross-Out], [1.0 ml] or [1.5 ml] or [3.0 ml] or [4.5 ml], Active Ingredients: Cyphenothrin 40.0%; Other Ingredients: 60.0%

BACK PANEL -

READ DIRECTIONS/PRECAUTIONS BEFORE USING.
CAUTION: KEEP OUT OF REACH OF CHILDREN
EPA REG. NO. 2517-XX

Revised 06/16/2004:
S:\Main\Sergeant's Pet Products\Labels\Sergeant's Cyphenothrin Squeeze-On For Dogs.

FEE

DATE OUT: 03/FEB/2005

FEE: PRODUCT CHEMISTRY REVIEW OF: Manufacturing-Use [ ] End-Use Product [X]
DP BARCODE: D305947 **EPA RECEIVED DATE:** 27/JUL/2004 **FILE SYMBOL/REG:** 2517-IN
PRODUCT: Sergeant's Cyphenothrin+IGR Squeeze-On For Dogs **MRID** 461661-01 & -02 **ACTION** R31
COMPANY : Sergeant's Pet Care Products, Inc. **NON-FOOD USES [X] DECISION NO.:** 338118
PPC NUMBER OF THE TGAIsIN THE PRODUCT: 129013, 129032

FROM: Sami Malak, Chemist
Technical Review Branch/RD (7505C)

TO: 13 George LaRocca/Linda DeLuise
Insecticide Branch/RD (7505C)

INTRODUCTION:

In a letter dated 15/JUN/2004, Brazos Associates, Inc. an agent for the applicant requested registration of subject product. In support of this action, the applicant included product chemistry data, a proposed label, a proposed basic CSF dated 29/DEC/2003, Formulator's Exemption, Certificate with respect to Citation of Data, and data Matrix..

FINDINGS:

1a. The subject product was produced by a non-integrated formulation system, meaning that the two active ingredients in the product are registered. The product contains 40% Cyphenothrin, Reg. No [redacted] plus 2% Nylar, Reg. No. [redacted] "Manufacturing process infor

1b. The subject product, an insecticide, is intended for insect control infesting dogs and puppies older than 12 weeks.

2a. The applicant should be advised to submit product chemistry data requirements pertaining to the storage stability (GRN 830.6317) and corrosion characteristics (GRN 830.6320) identified in this memorandum as data gaps.

2b. Except for the data gaps in Finding 2(a) above, the submitted/referenced product chemistry data is adequate and support registration of subject product.

3. Adequate analytical method is available for enforcement. The method was previously submitted and reviewed in connection with registration of the technical sourcess, Cyphenothrin, Reg. No. [redacted] and Nylar, reg. No. [redacted] "Manufacturing process infor

4. The label claim nominal concentrations of 40% Cyphenothrin plus 2% Nylar are consistent with that in the submitted basic CSF dated 16/JUN/2004, both are in compliance with the regulations of PR Notice 91-2. Further, the storage and disposal statement and the physical or chemical hazards statement are in compliance with the regulations of 40CFR§156.78.

5. The proposed basic CSF dated 29/DEC/2003, was filled out correctly in compliance with the regulations of PR Notice 91-2. Further, the upper and lower certified limits are within the standard limits of 40CFR§158.175(b)(2). All ingredients claimed in the CSF are cleared for use in pesticide formulations intended for non-food uses.

CONCLUSIONS: After resolving Finding 2(a) above, the TRB will have no objections for registration of subject product.

REVIEW OF PRODUCT CHEMISTRY DATA:

1. A statement of data confidentiality dated 29/DEC/2003 was included with this submission claiming confidentiality of some of the submitted data on the basis of its falling within the scope of FIFRA§10(d)(1)(A), (B), or (C). Review of CBI data has been removed to Confidential Appendix A.

2. A GLP statement dated 20/MAR/2003 was included with this submission to the effect that some of the submitted studies were conducted in compliance with the GLP requirements of 40CFR§160.

DATA SUBMITTED

Group A, Series 830-Product Identity, Composition, and Analysis (40 CFR 155, 160, 162, 167, 175 & 180)

830-1550 Product Identity and Composition

This product contains two registered technical grade of an active ingredients plus cleared inert ingredients intended for non-food uses (refer to product's basic CSF dated 29/DEC/2003).

830-1600 Description of Materials Used to Produce the Product:
Refer to Confidential appendix A.

830-1650 Description of Formulation Process:
Refer to Confidential appendix A.

830-1670 Discussion of Formation of Impurities:
Refer to Confidential appendix A.

830-1700 Preliminary Analysis:
Refer to Confidential appendix A.

830-1750 Certified Limits:
Refer to Confidential appendix A.

830-1800 Enforcement Analytical Method:

Adequate analytical method is available for enforcement. The method was previously submitted and reviewed in connection with registration of the technical sourcess, Cyphenothrin, Reg. No. [redacted] and Nylar, reg. No [redacted]

Identity, Composition, Formulation, and Analysis, Subgroup A, Series 830.1550 to 830.1800 (40 CFR 158.155 to 158.180)

Guideline Reference NO.(GRN 830.)/Title	Data Fulfilled	MRID No.
.1550 Product identity and composition	Y	461661-01
.1600 Description of materials used to produce the product	Y	461661-01
.1650 Description of formulation process	Y	461661-01
.1670 Discussion of formation of impurities	Y	461661-01
.1700 Preliminary analysis	Y	461661-01
.1750 Certified limits	Y	461661-01
.1800 Enforcement analytical method	Y	461661-01

Physical and Chemical Properties, Subgroup B, Series 830.6302 to -830.7300 (40 CFR 158.190)

Guideline Reference NO.(GRN 830.)/Title	Data Fulfilled	Value or Qualitative Description	MRID No.
.6302 Color	Y	Yellow.	461661-02
.6303 Physical state	Y	Liquid.	461661-02
.6304 Odor	Y	Odorless.	461661-02
.6314 Oxidation/seduction: Chemical incompatibility	NA	Does not contain an oxidising or reducing agents.	
.6315 Flammability/flame extension	Y	>200°F.	461661-02
.6316 Explodability	NA	Not considered to be explosive.	
.6317 Storage stability	G		
.6319 Miscibility	Y	Completely miscible in aromatics, petroleum distillates and alcohols. Immiscible in water.	461661-02
.6320 Corrosion characteristics	G	..	
.6321 Dielectric breakdown voltage	NA	It is not recommended for use around electrical equipment.	
.7000 pH	NA	Insoluble in water.	
.7100 Viscosity	Y	94.5 cps @ 23°C.	461661-02
.7300 Density/relative density/bulk density	Y	1.079 @ 24°C.	461661-02

Explanations: Y =The requirements were fulfilled; N = The requirements not fulfilled; N/A = Not applicable; G = Data gap; U = Requires upgrading; I = Incomplete or in progress; W = Waived.

Confidential Appendix A

830-1600 Description of Materials Used to Produce the Product:

Two registered technical grade of an active ingredients plus cleared inert ingredients intended for non-food uses (refer to product's basic CSF dated 29/DEC/2003).

830-1650 Description of Formulation Process:

[redacted]

830-1670 Discussion of Formation of Impurities:

The applicant reported no impurities $\geq$0.1% by weight were known to be formed during formulation and storage of the product. There was no chemical reaction in the process.

830-1700 Preliminary Analysis:

The submitted results of preliminary analysis agree with the label claim nominal concentrations of the active ingredients in the product.

830-1750 Certified Limits:

The applicant reported the same certified limits as those in product's CSF, a basic formulation dated 29/DEC/2003.

cc:S. Malak and Central File (Reg. No. 2517-IN).
7505C:RD:TRB:CM-2:Rm.268:s.m.03/FEB/2005:703-308-9365:<2517-IN>.

Brazos Associates, Inc.®

1806 Auburn Drive • Carrollton, Texas 75007-1451
Phone: 972-939-8390 • Facsimile: 972-939-8370
E-mail: marla@brazosassociates.com

By Overnight Courier Delivery

September 7, 2004

Document Processing Desk (PM-13)
Office of Pesticide Programs
U.S. Environmental Protection Agency
Room 266A, Crystal Mall #2
1801 South Bell Street
Arlington, VA 22202

Attn: Mr. George T. LaRocca
Product Manager Team 13

Dear Mr. LaRocca:

RE: Sergeant's Cyphenothrin Squeeze-On For Dogs
EPA File Symbol: 2517-IL

This submission of additional Efficacy Data is being made at the request of our client, Sergeant's Pet Care Products, Inc., and with respect to the above referenced pending registration.

With this submission we are providing the following:

1. EPA Application for Pesticide Registration (EPA Form 8570-1)
2. Revised EPA Data Matrix (Agency & Public File Copies)(EPA Form 8570-35)
3. Letter of Agent Authorization from Sergeant's Pet Care Products, Inc.

Should you have any questions or need additional information please do not hesitate to contact us.

Sincerely,

Marla K. Jackson
Agent for Sergeant's Pet Care Products, Inc.

cc: Mr. Larry Nouvel - Nouvel & Associates, Inc.

Please read instructions on reverse before completing form. Form Approved. OMB no. 2070-0060. Approval expires 2-28-95

United States
Environmental Protection Agency
Washington, DC 20460

- [ ] Registration
- [ ] Amendment
- [x] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number: 2517-IL
2. EPA Product Manager: George T. LaRocca
3. Proposed Classification: [ ] None [ ] Restricted
4. Company/Product (Name): Sergeant's Cyphenothrin Squeeze-On for Dogs
   PM#: 13
5. Name and Address of Applicant *(Include ZIP Code)*:
   Sergeant's Pet Care Products, Inc.
   2637 South 158 Plaza, Suite 100
   Omaha, NE 68130-1703
   [ ] *Check if this is a new address*
6. **Expedited Reveiw.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
   EPA Reg. No. _____
   Product Name _____

Section - II

- [ ] Amendment - Explain below.
- [ ] Resubmission in response to Agency letter dated _____
- [ ] Notification - Explain below.
- [ ] Final printed labels in repsonse to Agency lottor dated _____
- [ ] "Me Too" Application.
- [x] Other - Explain below.

Explanation: Uso additional page(s) if necessary. (For section I and Section II.)

Submission of addilional Efficacy Oata for registration support.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistent Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify) _____
* *Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Packago wgt. / No. per container	

3. Location of Net Contents Information: [ ] Label [ ] Container
4. Size(s) Retail Container
5. Location of Label Directions: [ ]
6. Manner in Which Label is Affixed to Product: [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Marla K. Jackson	Agent for Sergeant's Pet Care Products, Inc.	972-939-8390

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowlingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature: Marla K. Jackson
3. Title: Agent for Sergeant's Pet Care Products, Inc.
4. Typed Name: Marla K. Jackson
5. Date: 9/7/2004
6. Date Application Received (Stamped)

338

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Sergeant's
Pet Care Products, Inc.

March 11, 2004

Document Processing Desk (COADR)
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

Attn: Ms. Lois Rossi, Director
Office of Pesticide Programs – Registration Division

Dear Ms. Rossi:

Subject: Authorized Agents

Sergeant's Pet Care Products, Inc. (EPA Company Number: 2517) hereby appoints the following party as its primary agent of record to handle all registration matters on our behalf before the U.S. Environmental Protection Agency:

Mr. Steven E. Rogosheske
Rogosheske Consulting
1479 West Pond Road
Eagan, MN 55122

Phone: 651-330-1217
Fax: 651-330-1217
E-mail: srogo@comcast.net

In addition, representatives for the company named below are authorized to handle registration matters on behalf of Sergeant's Pet Care Products, Inc. including, but not limited to, filing of submissions, direct correspondence with Agency Officials via phone, fax, e-mail, etc., responding to or addressing other FIFRA related regulatory issues:

Brazos Associates, Inc.
1806 Auburn Drive
Carrollton, TX 75007-1451

Phone: 972-939-8390
Fax: 972-939-8370
E-mail: michael@brazosassociates.com

These appointments and authorization for Agent's supersedes all others as previously provided by Sergeant's Pet Care Products, Inc. (D.B.A. "Sergeant's Pet Products") and will remain in effect until revoked in writing by our firm. Should you have any questions, please do not hesitate to contact me.

Sincerely,

Joel Adamson
Senior Vice President Marketing

Notary Public

JO ANN KRENISKY
GENERAL NOTARIAL
SEAL
STATE OF NEBRASKA
Commission Expires
Sept. 28, 2006

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

DATA MATRIX

Date: 9/7/2004	EPA Reg. No./File Symbol: 2517-IL	Page 1 of 5
Applicant's/Registrant's Name & Address: Sergeant's Pet Care Products, Inc. 2637 South 158th Plaza, Ste. 100 Omaha, NE 68130-1703	Product: Sergeant's Cyphenothrin Squeeze-On for Dogs	

Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guidelines, Group A - Product Identity, Composition, and Analysis of Test Guidelines:					
830.1550	Product Identity and Composition	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1600	Description of Materials Used to Produce the Product	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1620	Description of Production Process	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1650	Description of Formulation Process	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1670	Discussion of Formation of Impurities	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1700	Preliminary Analysis		Not Applicable. Product is not a technical grade material and product is not produced by an integrated formulation system.		
830.1750	Certified Limits	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1800	Enforcement Analytical Method	46303801	McLaughlin Gormley King Company	PER	
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines:					
830.6302	Color	46303802	McLaughlin Gormley King Company	PER	
830.6303	Physical State	46303802	McLaughlin Gormley King Company	PER	
830.6304	Odor	46303802	McLaughlin Gormley King Company	PER	

Signature: Marla K. Jackson	Name & Title: Marla K. Jackson Agent for Sergeant's Pet Care Products, Inc	Date: 9/7/2004

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

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Applicant's/Registrant's Name & Address: Sergeant's Pet Care Products, Inc. 2637 South 158th Plaza, Ste. 100 Omaha, NE 68130-1703	Product: Sergeant's Cyphenothrin Squeeze-On for Dogs	

Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guidelines, Group A - Product Identity, Composition, and Analysis of Test Guidelines:					
830.1550	Product Identity and Composition	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1600	Description of Materials Used to Produce the Product	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1620	Description of Production Process	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1650	Description of Formulation Process	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1670	Discussion of Formation of Impurities	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1700	Preliminary Analysis		Not Applicable. Product is not a technical grade material and product is not produced by an integrated formulation system.		
830.1750	Certified Limits	46303801	Sergeant's Pet Care Products, Inc.	OWN	
830.1800	Enforcement Analytical Method	46303801	McLaughlin Gormley King Company	PER	
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines:					
830.6302	Color	46303802	McLaughlin Gormley King Company	PER	
830.6303	Physical State	46303802	McLaughlin Gormley King Company	PER	
830.6304	Odor	46303802	McLaughlin Gormley King Company	PER	

Signature: Marla K. Jackson

Name & Title: Marla K. Jackson
Agent for Sergeant's Pet Care Products, Inc

Date: 9/7/2004

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

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Date: 9/7/2004	EPA Reg. No./File Symbol: 2517-IL	Page 2 of 5
Applicant's/Registrant's Name & Address: Sergeant's Pet Care Products, Inc. 2637 South 158th Plaza, Ste. 100 Omaha, NE 68130-1703	Product: Sergeant's Cypenothrin Squeeze-On for Dogs	

Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines - Continued:					
830.6313	Stability to Normal and Elevated Temperatures Metals, and Metal Ions		Not Applicable. Not a technical grade product.		
830.6314	Oxidation/Reduction: Chemical Incompatibility		Waiver Requested: Product contains no oxidizing/reduction agents. Further, product is packaged in small (1 to 4.5 ml) containers for single/one time application both of which minimize the potential for contact with other products or materials.		
830.6315	Flammability	46303802	McLaughlin Gormley King Company	PER	
830.6316	Explodability		Waiver Requested: Based on flash point of >201°F, lack of potentially explosive formulation components, and limited package quantity (1 to 4.5 ml) there is no explosive potential.		
830.6317	Storage Stability		A 1-year Storage Stability Study with 0, 3, 6, 9 and 12 month analysis intervals is currently being conducted on behalf of Sergeant's Pet Care Products, Inc. by McLaughlin Gormley King Company and will be submitted to the Agency on completion.		
830.6319	Miscibility		Not Applicable. Product is not labeled for nor intended to be mixed with petroleum solvents.		
830.6320	Corrosion Characteristics		Test is running in conjunction with Storage Stability Study.		

Signature: Marla K. Jackson	Name & Title: Marla K. Jackson Agent for Sergeant's Pet Care Products, Inc	Date: 9/7/2004

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

DATA MATRIX

Date: 9/7/2004	EPA Reg. No./File Symbol: 2517-IL	Page 2 of 5
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Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines - Continued:					
830.6313	Stability to Normal and Elevated Temperatures Metals, and Metal Ions		Not Applicable. Not a technical grade product.		
830.6314	Oxidation/Reduction: Chemical Incompatibility		Waiver Requested: Product contains no oxidizing/reduction agents. Further, product is packaged in small (1 to 4.5 ml) containers for single/one time application both of which minimize the potential for contact with other products or materials.		
830.6315	Flammability	46303802	McLaughlin Gormley King Company	PER	
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830.6319	Miscibility		Not Applicable. Product is not labeled for nor intended to be mixed with petroleum solvents.		
830.6320	Corrosion Characteristics		Test is running in conjunction with Storage Stability Study.		

Signature: Marla K. Jackson	Name & Title: Marla K. Jackson Agent for Sergeant's Pet Care Products, Inc	Date: 9/7/2004

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

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DATA MATRIX

Date: 9/7/2004	EPA Reg. No./File Symbol: 2517-IL	Page 3 of 5
Applicant's/Registrant's Name & Address: Sergeant's Pet Care Products, Inc. 2637 South 158th Plaza, Ste. 100 Omaha, NE 68130-1703	Product: Sergeant's Cypcnothrin Squeeze-On for Dogs	

Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines - Continued:					
830.6321	Dielectric Breakdown Voltage		Not Applicable. Product is not labeled for use or intended for use around electrical equipment.		
830.7000	pH		Not Applicable. Product is insoluble in water; thus, not dispersible with water.		
830.7050	UV/Visible Absorption		Not Applicable. Product is not a pure active ingredient.		
830.7200	Melting Point/Melting Range		Not Applicable. Product is not a pure or technical grade material.		
830.7220	Boiling Point/Boiling Range		Not Applicable. Product is not a pure or technical grade material.		
830.7300	Density/Relative Density/Bulk Density	46303802	McLaughlin Gormley King Company	PER	
830.7370	Dissociation Constants in Water		Not Applicable. Product is not a pure active ingredient.		
830.7520	Particle Size, Fiber Length, and Diameter Distribution		Not Applicable. Product physical state is a liquid.		
830.7550	Partition Coefficient (n-octanol/water), Shake Flask Method		Not Applicable. Product is not a non-polar organic pure active ingredient.		
830.7560	Partition Coefficient (n-octanol/water), Generator Column Method		Not Applicable. Product is not a non-polar organic pure active ingredient.		
830.7570	Partition Coefficient (n-octanol/water), Estimation by Liquid Chromatography		Not Applicable. Product is not a non-polar organic pure active ingredient.		

Signature: /Marla K. Jackson/	Name & Title: Marla K. Jackson Agent for Sergeant's Pet Care Products, Inc	Date: 9/7/2004

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

DATA MATRIX

Date: 9/7/2004	EPA Reg. No./File Symbol: 2517-IL	Page 3 of 5
Applicant's/Registrant's Name & Address: Sergeant's Pet Care Products, Inc. 2637 South 158th Plaza, Ste. 100 Omaha, NE 68130-1703	Product: Sergeant's Cypenothrin Squeeze-On for Dogs	

Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines - Continued:					
830.6321	Dielectric Breakdown Voltage		Not Applicable. Product is not labeled for use or intended for use around electrical equipment.		
830.7000	pH		Not Applicable. Product is insoluble in water; thus, not dispersible with water.		
830.7050	UV/Visible Absorption		Not Applicable. Product is not a pure active ingredient.		
830.7200	Melting Point/Melting Range		Not Applicable. Product is not a pure or technical grade material.		
830.7220	Boiling Point/Boiling Range		Not Applicable. Product is not a pure or technical grade material.		
830.7300	Density/Relative Density/Bulk Density	46303802	McLaughlin Gormley King Company	PER	
830.7370	Dissociation Constants in Water		Not Applicable. Product is not a pure active ingredient.		
830.7520	Particle Size, Fiber Length, and Diameter Distribution		Not Applicable. Product physical state is a liquid.		
830.7550	Partition Coefficient (*n*-octanol/water), Shake Flask Method		Not Applicable. Product is not a non-polar organic pure active ingredient.		
830.7560	Partition Coefficient (*n*-octanol/water), Generator Column Method		Not Applicable. Product is not a non-polar organic pure active ingredient.		
830.7570	Partition Coefficient (*n*-octanol/water), Estimation by Liquid Chromatography		Not Applicable. Product is not a non-polar organic pure active ingredient.		

Signature: Marla K Jackson	Name & Title: Marla K. Jackson Agent for Sergeant's Pet Care Products, Inc	Date: 9/7/2004

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
Washington, D.C. 20460

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DATA MATRIX

Date: 9/7/2004	EPA Reg. No./File Symbol: 2517-IL	Page 4 of 5
Applicant's/Registrant's Name & Address: Sergeant's Pet Care Products, Inc. 2637 South 158th Plaza, Ste. 100 Omaha, NE 68130-1703	Product: Sergeant's Cypenothrin Squeeze-On for Dogs	

Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 830 - Product Properties Test Guideline, Group B - Physical/Chemical Properties Test Guidelines - Continued:					
830.7840	Water Solubility, Column Elution Method; Shake Flask Method		Not Applicable. Product is not a pure active ingredient.		
830.7860	Water Solubility, Generator Column Method		Not Applicable. Product is not a pure active ingredient.		
830.7950	Vapor Pressure		Not Applicable. Product is not a pure active ingredient.		
Series 870 - Health Effects Test Guidelines, Group A - Acute Toxicity Test Guidelines:					
870.1100	Acute Oral Toxicity	46166103	McLaughlin Gormley King Company	PER	
870.1200	Acute Dermal Toxicity	46166104	McLaughlin Gormley King Company	PER	
870.1300	Acute Inhalation Toxicity		Waiver Requested: Please refer to justification outlined in "Volume 3 of 3 of Submission" entitled: *"Sergeant's Cyphenothrin Squeeze-On for Dogs Waiver Request from the Requirement to Conduct Acute Inhalation Data - 870.1300"*		
870.2400	Acute Eye Irritation	46166105	McLaughlin Gormley King Company	PER	
870.2500	Acute Skin Irritation	46166106	McLaughlin Gormley King Company	PER	
870.2600	Skin Sensitization	46166107	McLaughlin Gormely King Company	PER	

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Agent for Sergeant's Pet Care Products, Inc

Date: 9/7/2004

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Ingredient: Cyphenothrin

Guideline Ref. Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Series 870 - Health Effects Test Guidelines, Group F - Special Studies Test Guidelines:					
870.7200	Companion Animal Safety	46166108	Sergeant's Pet Care Products, Inc.	OWN	
Series 810 - Product Performance Test Guidelines, Group C - Invertebrate Control Agent Product Performance Test Guidelines:					
810.3300	Treatments to Control Pests of Humans and Animals: *"Efficacy Evaluation Against Adult Cat Fleas (CTENOCEPHALIDES FELIS), Adult Brown Dog Ticks (RHIPICEPHALUS SANGUINEUS), American Dog Ticks (DERMACENTOR VARIABILIS), Nymphal Deer Ticks (IXODES SCAPULARIS), and Adult (AEDES AEGYPTI) Mosquitoes on Dogs".*	46166109	Sergeant's Pet Care Products, Inc.	OWN	
810.3300	Treatment to Control Pests of Humans and Animals	42614501 45086801 44948301 44546601	McLaughlin Gormley King Company	PER	
810.3300	*"Effect of Shampoo Application after Treatment with a Cyphenothrin Squeeze-On on Efficacy Against Adult Cat Fleas (Ctenocephalides felis), Adult Brown Dog Ticks (Rhipicephalus sanguineus) on Dogs".*	46298501	Sergeant's Pet Care Products, Inc.	OWN	
810.3300	*"Competitive Efficacy Evaluation of a Cyphenothrin Spot-On against Adult Cat Fleas (Ctenocephalides felis), Adult Brown Dog Ticks (Rhipicephalus sanguineus) and against Feeding by Aedes aloopictus and Culex quinquefasciatus Adult Mosquitoes on Dogs".*	46298502	Sergeant's Pet Care Products, Inc.	OWN	

Signature:	Name & Title: Marla K. Jackson Agent for Sergeant's Pet Care Products, Inc	Date: 9/7/2004

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Signature: Marla K. Jackson

Name & Title: Marla K. Jackson
Agent for Sergeant's Pet Care Products, Inc

Date: 9/7/2004

2517-IL

James Messina <jmessina@exponent.com>
02/13/2006 04:29 PM

To Linda DeLuise/DC/USEPA/US@EPA
cc George LaRocca/DC/USEPA/US@EPA, Rick Tinsworth <rtinsworth@exponent.com>
bcc
Subject Pending Cyphenothrin Registration

Linda,

I know we are working on risk assessment issues related to the pending Sergeant's cyphenothrin spot-on registrations. While we are working on those issues we wanted to know if there are any reviews (efficacy, tox, product chemistry) available for 2517-IN and 2517-IL) and 2517-OW. If so, can you please forward them to my attention.

I look forward to hearing from you.

Best Regards,

[illegible]

James Messina
Managing Regulatory Consultant
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Suite 1100
Washington, DC 20036
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